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A Journal of Neurology

EDITED BY

HENRY HEAD M.D. F.R.S.

WITH THE HELP OF

BYROM BRAMWELL, M.D.
THOMAS BUZZARD, M.D.
SIR DAVID FERRIER, M.D.,
F.R.S.

SIR WM. GOWERS, M.D., F.R.S.
F. W. MOTT, M.D., F.R.S.
R. PERCY SMITH, M.D.
C. S. SHERRINGTON, F.R.S.

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BRAIN.

PART I., VOL. 37.

THE CLINICAL ASPECTS OF SYPHILIS OF THE NERVOUS SYSTEM IN THE LIGHT OF THE WASSERMANN REACTION AND TREATMENT WITH NEOSALVARSAN.¹

BY HENRY HEAD, M.D., F.R.S.

Physician to the London Hospital

AND

E. G. FEARNSIDES, M.D.

*Assistant Physician to the Maida Vale Hospital for Epilepsy and Paralysis ;
Late Registrar to the London Hospital.*

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¹ The substance of this work was given in the Schorstein Memorial Lectures, delivered at the London Hospital on March 19 and 26, 1914.

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THE following paper is the third of a series, which set forth the results of work carried out in conjunction with Dr. Fildes and Dr. McIntosh on the behaviour of the Wassermann reaction in diseases of the central nervous system. In the first communication laid before the International Congress of Medicine in August, 1913 [10], we dealt clinically and pathologically with the conception of "parasyphilis." The second paper by Fildes and McIntosh [3] described the technique of the Wassermann reaction employed by them, and the results obtained in cases of nervous disease of syphilitic origin.

We shall now discuss the clinical aspects of this work and attempt to substantiate certain conclusions we have reached concerning the classification of these syphilitic diseases, their prognosis and treatment.

In all these papers the numbers appended to the cases remain the same, so that wherever any one number appears it always refers to the same patient.

We are much indebted to Dr. R. Donald, who made all the cell-counts mentioned in this work. The method he uses of measured drops not only ensures great accuracy, but also provides permanent preparations [2].

CHAPTER I.—INTRODUCTION.

Clinical medicine consists in the discrimination and classification during life of the phenomena evoked by pathological processes. The categories which emerge are spoken of as diseases. But the aim of such differentiation is to recognize the morbid process underlying the clinical manifestations for the purpose of treatment and prognosis; not infrequently, however, two conditions, apparently identical at the bedside, turn out to have a fundamentally different pathology. Thus, many patients with multiple syphilis of the nervous system are still

diagnosed as cases of disseminated sclerosis, a disease that stands in no relation to the *Spirochæta pallida*. Here the Wassermann test has enabled us to distinguish two diseases, often confused with one another, and this growth of knowledge has in turn been followed by closer clinical discrimination of signs and symptoms. On the other hand, two apparently different diseases, from the clinical aspect, may turn out to be based upon an identical morbid process. In such cases intermediate forms can be discovered between the two diseases, so that in some instances it may be impossible to say to which category a particular patient belongs. No two diseases could be more different, at first sight, than the classical forms of dementia paralytica and tabes dorsalis; and yet both are due to an identical pathological process attacking different parts of the central nervous system. A host of intermediate forms, necessitating the invention of the term "tabo-paresis," bear witness to the absence of a sharp line of demarcation between the two conditions, which depend for their clinical diversity solely on the anatomical incidence of the pathological process.

It has long been recognized that the manifestations of chronic syphilis of the nervous system cannot be separated into "diseases." In any one case symptoms and signs usually point to a simultaneous affection of both brain and spinal cord. We speak of encephalitis, myelitis, &c., according to the site of the principal lesion; but in the majority of instances careful clinical observation reveals signs pointing to affection of some other part of the nervous system. Thus a patient with myelitis may have pupils that do not react to light; hemiplegia may be accompanied by signs of a lesion of the spinal nerve-roots, or bulbar symptoms may be associated with a disturbance of micturition. The morbid process underlying all the conditions is the same; they are different manifestations of the same disease.

Until recently, however, it was universally held that the pathological process, underlying these cases of chronic syphilis, differed fundamentally from that in "parasyphilis" of the nervous system. Fournier invented the term to signify a condition which required syphilis as an antecedent, but was not itself an active manifestation of the syphilitic virus. This conception he based on the refractory nature of "parasyphilis" to treatment with anti-syphilitic remedies.

When, however, Noguchi demonstrated the presence of the *Spirochæta pallida* in the brain of patients who had died from dementia paralytica, the first half of Fournier's contention fell to the ground. Moreover McIntosh and Fildes have proved that little, if any, arsenic enters

the substance of the central nervous system after the injection of salvarsan or neosalvarsan, and so gave a more probable explanation of the insusceptibility of "parasyphilis" to such remedies. "Parasyphilis" is refractory to treatment, not because it depends on a different pathological process, but because the virus is active in parts that are not reached by the drug in effective doses.

The difference between chronic syphilis of the nervous system and "parasyphilis" is not a difference of morbid process but of anatomical situation and chemical permeability; for the deeper the virus lies in the substance of the central nervous system, the less will it be reached by treatment which readily acts on the same process affecting vessels and meninges.

But although "parasyphilis" of the nervous system is at bottom simply another manifestation of syphilitic spirochætosis, we believe that the conditions, classed under this head, require a previous sensitization of some part or parts of the central nervous system. This antecedent preparation of the tissues is also required for the formation of a gumma, and both "gummatosis" and "parasyphilis" are manifestations of the activity of the spirochæte in tissues that have become hypersensitive during previous stages of the infection. The difference between them lies in the tissues attacked. In the one case it is the meninges and vessels, in the other the reaction to the spirochæte occurs in the neuroglia and essential nerve-structures.

It is universally recognized that the reaction which forms what we call a gumma is out of all proportion to the number of spirochætes that can be discovered within it. In the same way we suspect that the difference between the clinical course of cases of "parasyphilis" and of the acuter forms of cerebrospinal syphilis lies in the extent to which the central nervous system has become hypersensitive.

We shall show that it is quite impossible, in many cases, to diagnose the difference between syphilitic encephalitis and dementia paralytica without observing the effect of treatment and the changes it produces in the Wassermann reaction. In the same way syphilitic meningo-myelitis may simulate tabes dorsalis, or may evoke signs and symptoms that closely resemble amyotrophic lateral sclerosis.

All these categories of disease have been destroyed by recognition that the pathological process is the same in nature though different in the site of its activity and the condition of the tissues on which it acts. We shall attempt in this paper to show how a reconsideration of the clinical signs and symptoms, aided by the Wassermann reaction,

can lead us from this chaos to diagnosis of the site of the lesion and to recognition of the probable behaviour of the disease.

First of all, however, it will be necessary to consider nomenclature in the light of these conceptions of syphilitic disease of the nervous system. We cannot hope to obtain a post-mortem examination in any but a minute proportion of the patients under observation; for many recover, and most of those who die drift off into Asylums and Work-house Infirmaries where they excite little interest.

All names given to such diseased conditions must correspond to clinically demonstrable states. If the signs point to affection of a series of posterior nerve-roots some meningitis must be present and in the same way a sudden hemiplegia signifies in most cases vascular disease. Similarly loss of recognition of posture and want of appreciation of the vibrating tuning-fork indicate destruction of the posterior columns, which, if widespread, show that a lesion is situated in the substance of the spinal cord.

Then, again, by watching the behaviour of the disease after intravenous injections of neosalvarsan or allied drugs, we are able to recognize if it is amenable to treatment or not. When rapid improvement occurs not only in symptoms and signs, but also in the Wassermann reaction in the cerebrospinal fluid, we can be certain that the lesion is situated in parts, such as the meninges and vessels, easily reached by a drug circulating in the blood. But no improvement in the clinical condition, accompanied by a positive Wassermann reaction in the cerebrospinal fluid, unchanged over months or years, points to an affection of the deeper structures of the nervous system, which are nourished by fluids not reached effectively by the arsenical compounds employed according to the present methods.

All nomenclature must, for the present, depend on the interpretation of phenomena which are clinically recognizable, and must not be based on hypothetical pathological states. Thus "tertiary" or "gummatous" must not be applied to clinical conditions, and it will be wiser to get rid altogether of the word "parasyphilis," because it conveys a false pathological conception and gives no indication of the form or nature of the clinical manifestations in any case to which it may be applied.

We propose, therefore, to divide cases of syphilitic disease of the central nervous system into those of syphilis meningo-vascularis and syphilis centralis. The meaning of the first name is obvious, for in many cases we know from clinical observation that the meninges and vessels must be affected. Syphilis centralis was chosen to include all

those cases where the degeneration of nerve-tracts or nuclei shows that the lesion must lie within the structure of the nervous system itself. This category includes "parasyphilis," used in the strict sense for those forms of the disease which are not materially influenced by our present methods of anti-syphilitic treatment. The name syphilis centralis was selected in preference to "parenchymatous" syphilis, favoured by so many speakers at the International Medical Congress, because we wish to lay stress on the reaction to the syphilitic virus of both the neuroglia and essential nerve structures (McIntosh, Fildes, Head and Fearnside [10]). We are not at variance in any way with those who speak of "parenchymatous" syphilis, but believe the term syphilis centralis is less likely to lead, in the future, to the erroneous view that the nerve elements alone react in these cases to the toxic action of the spirochæte.

CHAPTER II.—THE HISTORY OF INFECTION.

Before the coming of the Wassermann reaction it was impossible to be certain that the patient had been infected in the past without a history of chancre, rash, sore throat, or other signs of syphilis. Every physician recognized that undoubted late manifestations, such as tertiary lesions or tabes dorsalis, might appear in persons who honestly denied all knowledge of infection. This cast an uncomfortable shadow of doubt over all diagnosis in chronic diseases of the nervous system, which has been dispersed by the employment of the quantitative estimation of the strength of the Wassermann reaction in the serum and cerebrospinal fluid. It will be well, therefore, to review this question in the light of the histories we have obtained in the patients investigated for this research.

But first of all we wish to endorse the experience of Erb, and later of Nonne, that conscious denial of infection is uncommon, provided the patient is questioned quietly and with reasonable precautions. It is absurd to suppose that a man will be truthful if he is questioned in a public ward before students and nurses, especially when he may himself have some doubt as to his answer. Again we are not likely to obtain a detailed account of his infection from a patient with dementia paralytica or other brain disease which destroys the memory. But, if after his confidence has been gained the necessary questions are asked in a kindly and business-like manner, we have always discovered a remarkable desire on the part of the same patient to help us to determine the date of infection and its sequelæ.

On the other hand, in a woman it is neither possible nor desirable, in many cases, to probe the history of infection; we must rest satisfied with a positive Wassermann reaction and a history of illness or a series of miscarriages which occupied some period of her life.

Out of forty-seven males of the hospital class suffering from active syphilis of the nervous system, who were investigated for this research, thirty-nine admitted some sign of syphilitic infection and could give its approximate date. Four patients acknowledged gonorrhœa only, and four admitted exposure but denied all venereal disease.

Let us next consider the history of 70 patients with classical tabes dorsalis; of these 48 were seen by one of us in private practice and 22 were of the hospital class and appear in the records of this research. Amongst these 70 patients, 8 denied all venereal disease but confessed to frequent exposure, while 16 admitted gonorrhœa but denied all syphilitic infection and showed no local scar.

Thus amongst 117 males, all of whom demonstrably suffered from syphilis of the nervous system, 12 denied all venereal disease (10 per cent.); these are the cases of "syphilis d'emblée," where the infection occurs without local reaction. At the same time the general infection was so wanting in virulence, or the reaction of the body was so effective, that it was apparently not followed by such manifestations as a rash, sore throats, or fall of hair.

A more important group from the clinical point of view is formed by the 20 cases (17 per cent.) where the syphilitic infection ran its course under cover of a gonorrhœa. It would seem as if, in some persons, the gonorrhœal inflammation had permitted general infection with the spirochæte to occur without the obvious formation of a specific local reaction.

CHAPTER III.—EARLY SYMPTOMS AND SIGNS OF CEREBROSPINAL SYPHILIS.

To clinicians who have not interested themselves particularly in neurology a diagnosis of syphilis of the nervous system evokes definite clinical pictures, as, for instance, that of a "myelitis." But such gross diseases are usually the final stage of a process which has previously manifested itself in a host of minor conditions that usually pass unrecognized. It is, however, in this early stage that the disease is amenable to treatment; for the symptoms and most of the signs which accompany a "myelitis" are due to secondary destructive processes, such

as hæmorrhage, and cannot be materially affected by anti-syphilitic remedies.

This chapter will therefore be devoted to a consideration of the early symptoms and signs of cerebrospinal syphilis. We have excluded all cases that would be usually called "parasyphilis," such as classical examples of tabes dorsalis, because we hope to show how frequently these disturbances of function anticipate the better known and graver signs of cerebrospinal syphilis. Everyone is familiar with the occurrence of root-lesions in the course of tabes dorsalis, but they are less often recognized as the precursor of syphilitic disease of the spinal cord and its membranes.

Early diagnosis means the certain recognition, before the onset of grave destructive changes, that the more or less trivial signs and the symptoms of which the patient complains are due to active syphilitic spirochætosis. A few years ago the acute clinician might suspect the true origin of the headaches, shivering attacks, malaise, pupillary abnormalities or curious radicular changes in sensation; but now the perfection of the Wassermann reaction has converted such a hypothetical diagnosis into a certain one. Moreover, the fact that we can be sure, in many cases, of the syphilitic origin of these morbid states has made it possible to study them with greater precision, and to obtain a clearer clinical view of the conditions under which they appear and the significance of their occurrence.

§ 1.—*Changes in Personality and Aptitude.*

One of the earliest alterations produced by the activity of cerebrospinal syphilis is a change for the worse in character and personality. A skilled workman ceases to be worth his high wages. The steward of a golf course found that he could not remember the many little details necessary to the success of his day's work (No. 3, p. 34). A Jewish baker "lost all his manners at home and could not be trusted to carry out completely the processes of the bakehouse." A fireman on the railway lost his job because he used to fall asleep during his hours of duty (No. 59, p. 37). In one case, where we previously knew the patient, we readmitted him to hospital solely on a change in his manner, greatly to his own surprise; the Wassermann reaction, and subsequent closer clinical examination in the wards, justified our diagnosis that he had relapsed. The patients who formed the material of our research were solely those who came to a General

Hospital, and did not include the insane. The mental changes we were able to observe appeared in the course of some gross physical manifestation of syphilis of the central nervous system. In some cases they passed away as the graver signs developed and, in most instances, they yielded rapidly to treatment. Though slight they were very common amongst the class of patients with whom we have had to deal.

Attention and the power of concentration commonly suffer and the patient can no longer carry through a full day's work; moreover he is liable to make mistakes in details with which he has long been familiar. Memory for recent events becomes uncertain and capricious, because he cannot concentrate his attention upon them at the time with sufficient intensity.

These patients frequently become highly emotional and untrustworthy in their social relations. That balance between emotion and reason, which forms the basis of individual personality, is disturbed. They are "not themselves" and become uncertain and hesitating in action.

In this condition they are commonly thought to suffer from neurasthenia, and the organic basis for the symptoms is not suspected until too late for effective treatment.

A Case of Supposed Neurasthenia with a Negative Wassermann Reaction in the Serum, but a Positive Reaction and an Increase of Cells in the Cerebrospinal Fluid.

Case 123.—G. P., male, single, clerk; born in 1885. In November, 1910, at the age of 25, he contracted syphilis and suffered from a chancre for which he was treated with mercurial pills from December, 1910, to October, 1911.

Twelve months after infection, in November, 1911, a crop of warty spots appeared on his forehead, face and neck, and persisted for fourteen days. Some time before Christmas, 1911, he developed a weeping eczema on the legs, forearms and dorsum of his hands, and in December, 1911, his tongue became ulcerated. He then attended the skin department of the London Hospital under the care of Dr. J. H. Sequeira, and was injected with two doses of 0.6 gm. of salvarsan. Under this treatment the ulceration of his tongue healed rapidly; the eczema, however, persisted unchanged. During the months from March to October, 1912, except for the eczema, he remained in good health.

Within two years of infection, however, he began to complain of left-sided frontal headache, and in November, 1912, was sent to Dr. Fildes and Dr. McIntosh for further examination of the blood and cerebrospinal fluid. On November 25, 1912, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 4.4.1.0.0.}$ and the cells in the cerebrospinal fluid were 85 per cubic millimetre. And yet at this time the most careful examination in the Hospital failed to reveal any signs of disease of the central nervous system.

He did not come under our observation between November 29, 1912, and May, 1913. But when he was again admitted on May 28, 1913, he had become neurasthenic, introspective and less rational in his habits; at the same time his capacity for business had failed.

He complained that on May 18 he had caught a "chill," which was followed by acute pain in the left chest "around the heart." This pain was followed by shortness of breath, but he did not suffer with a cough and there was no expectoration. On examination in the Hospital (May 28, 1913) movement was defective at the base of the left half of the chest, the percussion note was impaired and the air entry defective. The heart was not displaced. X-ray examination of the chest showed some doubtful obscuring of the left half of the diaphragm. The lungs themselves were completely unaffected. We were thus left in doubt as to whether the pain was of root origin or whether it was due to a pleurisy at the left base.

Mentally the patient was very unstable; he was emotional and irritable; he resented questions and gave illogical answers. No hallucinations or delusions were present. He slept badly and complained of severe general headaches, referred chiefly to the occipital region and the back of the neck.

The fundi appeared natural. All ocular movements were well carried out. The pupils reacted well to light and accommodation. Motion was unaffected. No disturbance of sensation could be detected. The reflexes, sphincters and spine were unaffected.

No abnormal signs were detected in the heart or abdomen. The urine contained neither albumen nor sugar.

On June 6, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.2.}{\text{cs.f. } 4.4.4.4.3.}$ and the cells numbered 90 per cubic millimetre.

He was injected on June 6, 1913, with 0.6 gm. of neosalvarsan, on June 12, on June 18, on June 23, and on July 26 with 0.9 gm.

On August 13, 1913, the Wassermann reaction was $\frac{\text{serum } 4.3.2.0.0.}{\text{cs.f. } 4.4.4.0.0.}$ and the cells were 3 per cubic millimetre; he was then injected again with 0.9 gm. of neosalvarsan.

Under this treatment his mental state improved rapidly and the pains in his chest disappeared; by the end of September, 1913, he would have passed both mentally and physically as completely normal.

On September 24 and on November 15, he was injected with 0.9 gm. of neosalvarsan.

On November 15, 1913, the Wassermann reaction in the serum was again completely negative.

On January 28, 1914, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 4.2.0.0.0.}$ and the cells numbered 5 per cubic millimetre.

Occasionally, however, the first intimation that syphilis has attacked the central nervous system is a slowly increasing dementia. The

patient "sits about" listlessly, unwilling to begin either work or play. He cannot remember when or where he was born, his age, or the details of his recent life. He sleeps the greater part of the day and resents being roused; occasionally the condition may resemble that of dementia præcox, but none of our patients have shown true negativism (cf. Plaut [18], p. 55).

An Instance of the Cerebral Form of Cerebrospinal Syphilis.

Case 284.—R. M., male, married, clerk; born 1887. In 1905, at the age of 18, this patient contracted syphilis and suffered from a "running which lasted a few weeks only," followed by a succession of bad throats, but no rash. He was treated for gonorrhœa only. Two years later he began to have attacks of "rheumatic pains" in the legs; these passed away without treatment. In 1907 he married. After marriage he remained well until the beginning of 1913. His wife has miscarried three times and there are no living children.

About April, 1913, ten months before he first came under observation, his employers noticed that he had become less trustworthy and less certain in business, and his wife stated that about the same time he became more irritable at home.

On December 17, 1913, whilst adding up the accounts in the office, he had a seizure, "he came over giddy and felt numb all down the left side"; the attack itself lasted about ten minutes. Afterwards the left side of his face was drawn up and his speech altered. He then began to suffer from intense generalized headaches; these would come on in attacks which always seemed to affect the left half of the body and made him unable to hold small objects in his left hand. One day, early in January, 1914, whilst walking in the street, he had a second seizure. A sudden pain seemed to start in the left forearm, shoot into the left hand and then pass into the left axilla. The pain made him feel giddy, but he did not actually fall. He was helped to a tram and went home to bed. After the attack the whole of the left half of the body, face, arm, leg and trunk seemed numb, and the left leg became weak. He continued at work until February 20, 1914. On that day, whilst watching a gymnastic exhibition, he became very excited and had a third seizure, accompanied again by much giddiness, and followed by a feeling of weakness and numbness in the left half of the body, face and extremities. After the first seizure he had experienced at various times some difficulty in passing urine; either he had had to wait after desire came or else he had had to hurry to avoid wetting himself. Memory and aptitude in business failed. After December, 1913, he could no longer be trusted to do his work up to the old standard, and he found difficulty with his accounts. He became depressed and at home was restless and irritable. The headaches became extremely troublesome and would last in attacks over a period of days. He also complained of much giddiness with nausea and feelings of inability to concentrate at work. From time to time he had been subject to shooting pains in the occipital region and more especially

in the back of the neck. He had slept badly, but at the same time had often fallen asleep when at his work. At nights "sleep was disturbed and never seemed to rest me." When walking the left leg felt "dead and useless."

He first came under observation on February 23, 1914. No abnormality was discovered in the heart, lungs, abdomen, or urine.

The patient was a well-informed, intelligent man. Attention was fleeting and erratic. He disliked all restraint and was restless and irritable over the restrictions of hospital routine. Memory for recent events was extremely defective, but was little impaired for those of long ago. Writing was unsteady and the letters were badly formed. Speech was definitely affected; the syllables were slurred and the words badly pronounced.

He complained of a throbbing headache in the frontal region and the occiput was tender to pressure. The headache led to a feeling of sickness, and he vomited on several occasions before treatment was begun. Vision was unimpaired, and the visual fields were of normal dimensions. The optic discs appeared natural but the veins of the fundus oculi were engorged. The other special senses were unaffected.

The pupils were large; reacted sluggishly to light but dilated on continued exposure; they reacted briskly to accommodation and convergence. The face showed little expression. The tongue was protruded straight, but could not be held steadily. Otherwise, no abnormalities were discovered in the territory of the cranial nerves.

The gait was rolling. Fine movements of the left hand were performed clumsily and the fingers on each side were badly aligned. No local muscular atrophy and no changes in muscular tone were discovered.

He complained of a curious numb feeling in the left half of the body, but no gross loss of sensibility was discovered on testing.

The knee-jerks and ankle-jerks were brisk and equal on the two sides. Ankle-clonus was not present. Both plantar responses were flexor. The abdominal reflexes were obtained with difficulty on both sides.

He complained of some difficulty in holding and in passing urine, and not infrequently wetted the bed.

On February 25, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.0.}$ and the cells numbered 65 per cubic millimetre. He was injected with 0.45 gm. of neosalvarsan on February 27, 1914, and with a similar dose on March 2. On March 4, and on March 7, 0.9 gm. of neosalvarsan were given.

By April 30, 1914, the patient returned to work mentally and physically a normal man.

§ 2.—*Disturbance of Sleep.*

All forms of disturbance of sleep may appear among the early symptoms of cerebrospinal syphilis. Occasionally the patient falls asleep on the most inopportune occasions, but more usually he becomes

sleepless. Insomnia is a common accompaniment of that state of emotional irritability mistaken for neurasthenia.

But in some cases the patient tends to fall into a "half-conscious sort of state" even in the day. He cannot rouse himself to take in what is going on around him. At night this condition takes the form of a mild delirium; thoughts race through his head and he may fall into a state resembling a mild confusional psychosis (Heubner [6], Oppenheim [16], p. 50, Plaut [18], p. 93).

In one case the patient complained that she was not "herself"; when it was dark she would see "strange sights" and thought "God was talking with her." "Horrible dreams," noises heard at night and even "ghosts" may be manifestations of this nocturnal state (No. 3, p. 34).

Occasionally the patient complains that the headache, so common in cerebrospinal syphilis, keeps him from sleep, and that he then sees "terrible things"; he lies awake full of fear and anxiety.

Such nocturnal psychoses are commoner than is usually supposed amongst sane patients suffering from syphilis of the central nervous system. They are obviously nothing but milder forms of that confusional insanity, accompanied by hallucinations, frequently associated with severe syphilitic encephalitis (Plaut [18], p. 27 *et seq.*).

Acute Syphilitic Encephalitis with Profound Mental Changes.

Death: Autopsy.

Case 183.—S. B., female, married; born 1880. This patient was admitted to the London Hospital, under the care of Dr. Russell Andrews, on May 8, was transferred to the care of Dr. Head on May 23, and died on May 30, 1913.

There was no definite history of any syphilitic infection, but her husband's serum gave a positive Wassermann reaction (4.4.4.1.0).

In 1898, at the age of 18, she married her first husband, who died, aged 20, three weeks after marriage, from "abscess on the brain." She then courted her second husband for three years, and married him in 1903; by him she was pregnant six times (1) a girl, born August, 1904; (2) a girl, born 1907; (3) a stillbirth at the eighth month; (4) a boy, born 1908; (5) a girl, born 1909; and (6) a child born in Hospital on May 8, 1913; five healthy children survived her death.

Since her second marriage she had always been subject to "fainting attacks," often two or three in the twenty-four hours, at any time of night or day; she complained of "feeling faint" and of "losing herself" momentarily in these attacks. With this exception she had had no illness since 1903, and all her five previous pregnancies had been uneventful.

In June, 1912, almost a year before her death, her memory was noticed to be failing; she made no complaint, but her friends said that she was "no longer herself." Shortly after this she would complain of hearing noises in the dark, and at night, and interpreted them as "bells" or "God talking with me." She also complained of seeing strange sights of various sorts in her own kitchen. From time to time between June and December, 1912, these hallucinations had worried her and her husband said that at times she had behaved "as if out of her mind."

In December, 1912, she discovered that she was again pregnant. About this time her husband lost his employment, and immediately his wife's mental condition seemed to improve. During the months between December, 1912, and April, 1913, her condition altered little, but the fainting attacks came on more frequently.

On May 6, 1913, she developed "epileptiform attacks," and was admitted to the Maternity Wards as "eclampsia." Before admission she had five of these attacks and became "dazed and funny." On admission labour had begun; a Champetier de Ribes' bag was inserted, and a healthy child, weighing 5 lb., showing no signs of congenital syphilis, was delivered six hours later. An examination of the urine on admission showed the presence of a cloud of albumen, and a positive reaction with ferric chloride, but no alteration in the ammonia-urca nitrogen ratio. The puerperium was uneventful, except for the fact that the patient at times talked irrationally; she complained of seeing strange objects in the ward after dusk and hearing noises "from under her bed." Slight pyrexia to 99° 8' F. (37° 6' C.) followed delivery, but the lochia were normal.

On May 18, 1913, ten days after delivery, the patient was allowed to get up. She then became subject to attacks of exaltation and of weeping. Examination at this stage showed that, though the pupils were of normal size, their reaction to light was extremely sluggish.

On May 23, 1913, she was transferred to the care of Dr. Head. At this time she complained of hearing voices, usually the voice of God telling her of her many misdeeds, or of the devil telling her to commit wrong. She said that the voices were all around her and constantly at work. Her emotional state varied, at one time she would laugh immoderately, at others she would be moved to tears.

Her memory was extremely bad; she could give no connected account of herself or of her previous health and habits. Speech was thick and slow and articulation was defective, syllables being missed out or badly slurred. She could not write and would not read either aloud or to herself.

She complained of no headache, and whilst under observation did not vomit.

Shortly after transfer to the medical ward she began to show attacks in which she clutched the bed-clothes or moved her arms to and fro wildly.

The special senses were unaffected, and the disc and fundus on both sides appeared healthy.

Ocular movements were well carried out. The pupils were equal in size, but reacted badly on exposure to light; the reaction obtained was ill-sustained. The left half of the face appeared flatter than the right, and in the lower half moved badly on volition. The tongue was protruded straight, but could not be held steadily. There was no tremor of the lips. The palate and larynx were unaffected.

No muscular paralysis was discovered and all movements could be carried out at will.

Owing to her mental state sensation could not be tested.

The tendon reflexes were all extremely brisk; ankle-clonus was not obtained, and the plantar responses were of the flexor type.

The sphincters and spine were unaffected.

On May 24 and 25 the condition altered but little. On the night of May 25 to 26, after a period of excessive restlessness, she had five epileptiform attacks accompanied by general convulsions, cyanosis and loss of consciousness.

On the morning of the 26th she was dull, somnolent, stuporous and sub-conscious, and could be roused only partially. The temperature rose to 103° F. (39·3° C.), and the rate of the pulse to 150 beats per minute, whilst respirations became rapid and sighing, 40 per minute. On examination on this day she was seen to have a divergent squint of the right eye.

During the next three days, the 27th, 28th and 29th, she remained dull and drowsy. She wasted rapidly, her orbits became sunken, bilateral purulent conjunctivitis and incontinence of urine set in. The temperature remained between 102° to 103° F. (38·5° to 39·3° C.), the rate of the pulse 112 to 130 and the respirations 44. Examination showed the persistence of the squint, but no complete paralysis of any eye muscle. The reflexes remained unaltered.

At 4 p.m. on May 29, 0·9 grm. of neosalvarsan were injected intravenously; the temperature and the rate of the pulse immediately fell and six hours later the general condition had apparently greatly improved. Twelve hours after the injection, however, the patient had an attack with cyanosis lasting fifteen minutes. She then seemed to recover and at 6 a.m. ate a good breakfast. At 7 a.m., however, respiratory failure again developed and seventy-five minutes later, despite the free administration of stimulants, she died.

On May 27, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.4.}}{\text{cs.f. 4.4.4.4.4.}}$ and the cells numbered 33 per cubic millimetre.

§ 3.—*Headache.*

All clinicians have laid stress on the frequency with which headache appears amongst the first symptoms of syphilis of the central nervous system; but too much emphasis has been laid on its nocturnal occurrence.

It is usually severe, paroxysmal, and lasts for several hours. Some patients speak of it as "maddening." In one instance it appeared three or four times a week in the evening, and lasted for twelve hours. The whole scalp may become tender so that the patient cannot wear a hard hat (No. 262, p. 62).

We have seen no patient in whom this headache was strictly and constantly localized to a particular portion of the head, and if tenderness is present it is usually widespread. Localized tenderness confined to a comparatively small area should lead to a careful search for a gumma of the skull or its coverings. In cases where such a gumma is present, for instance in the temporal region, a fan-shaped area of superficial tenderness can usually be discovered; this is wider towards the vertex and converges towards the point in the temporal region at which the gummatous thickening can usually be felt. This is due to irritation of the small nerve-trunks which spread out towards the periphery after passing through the area of gummatous inflammation. On the forehead a gumma causes a similar area of tenderness which extends directly backwards from the point at which it is situated.

Occasionally the headache of cerebrospinal syphilis is accompanied by nausea which may culminate in vomiting. This leads to much difficulty in diagnosis, and if optic neuritis is present the case may be thought to be one of cerebral tumour. In fact, the differential diagnosis between the two conditions, if the serum gives a positive Wassermann reaction and the cerebrospinal fluid a negative, may be one of extreme difficulty.

Headache, Vomiting and Optic Neuritis Three Years after Infection with Syphilis.

Case 122.—J. P., female, single, skirt hand; born 1893. This patient was infected with syphilis at Christmas, 1909, just before she was 17, and shortly afterwards began to suffer with headaches and recurrent sore throats. In August, 1910, she gave birth to a child, which died seven weeks later of congenital syphilis and wasting. Whilst pregnant she was treated for some time with mercury by the mouth.

From August, 1910, until August, 1912, she remained in fairly good health.

About August, 1912, she began to suffer from recurrent attacks of universal headache, usually worst in the morning and affecting chiefly the frontal region and upper portions of the face; the pains were described as "throbbing." When the headache was severe the scalp became tender. She kept at work until November, 1912, but gradually became more and more "tired and drowsy." The headaches then led to a continual feeling of sickness, but about the middle

of November first caused actual vomiting. She would vomit nearly every morning, and this at first relieved her headache.

On the morning of December 2, 1912, she awoke to find that her right eye had "turned in," and from that time until her admission on January 4, 1913, everything appeared "double." Vision gradually failed and all objects appeared misty and distorted.

Between August, 1912, and the date of her admission her menses had ceased, but she was not pregnant. On admission to the London Hospital in January, 1913, the patient was seen to be a small, undersized, pale, anæmic girl. The temperature was slightly raised and oscillated between 98° 8' F. and 99° 4' F. [about 37° 4' C.]. The rate of the pulse was rapid and usually about 100 beats per minute. The lymphatic glands in the posterior triangle of the neck on both sides and the epitrochlear glands were definitely enlarged. No rash was present and the tonsils and pharynx appeared healthy. No abnormal signs were discovered in the heart, lungs, abdomen or urine.

Mentally she was dull, stupid and slow. Speech was little affected. She complained of intense generalized headaches with pressure tenderness of the skull in the occipital and frontal regions. As an in-patient she complained of no nausea and she did not vomit.

Vision on both sides was defective, more especially for form: the patient complained that all outlines were distorted. Optic neuritis of moderate severity was present; the vessels were full and tortuous, the lamina cribrosa filled in and the edges of the disc blurred. About 3 D. of swelling was measured in each eye. Hearing, smell and taste were unaffected.

The patient complained of diplopia. On examination, all movements could be carried out, but the axes of the two eyes did not move together so as to produce binocular vision. The right eye moved outwards more sluggishly than the left. No ptosis or nystagmus was present. The left pupil was wider than the right; both reacted sluggishly to light, but readily to accommodation. The face was flat and expressionless. The tongue could not be held steadily. The cranial nerves were otherwise unaffected. There was no interference with motion, sensation or control of the sphincters.

The knee-jerks were readily elicited, ankle-clonus was not present, the abdominal reflexes were obtained and both plantar reflexes gave a flexor response.

On January 8, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 10 per cubic millimetre.

On January 10, January 17 and January 23, 1913, intravenous injections of 0.9 gm. of neosalvarsan were administered.

After treatment the anæmia disappeared, the glandular enlargement subsided and the mental condition of the patient improved. Vision became almost normal and seven days after the first injection the diplopia had passed away; from this time the headaches ceased.

This headache may exist for a considerable time as an isolated

manifestation, and we believe that in cases where the patient has been treated with success the reappearance of the characteristic headache is an invaluable sign of a "relapse."

§ 4.—*Shivering Attacks.*

Several instances have come under our notice in which shivering attacks, with or without fever, formed the earliest manifestation of syphilis of the central nervous system.

In the following case no cause could be found in the urinary tract, the lungs, or in any other organ for the shivering and malaise; for, although the first attack was accompanied by swelling of one testicle, this complication was not present in the severer attacks which followed. It is interesting to notice that symptoms of irritation of posterior roots finally made their appearance.

Recurrent Attacks of Shivering with Pyrexia, forming the earliest sign of Syphilis of the Central Nervous System.

Case 63.—W. G., male, married, railway shunter; born 1878. In 1895, at the age of 17, this patient caught syphilis and suffered from a chancre and rash; he was treated for six weeks.

Thirteen years later, about Christmas, 1908, he began to complain of "shivering attacks," aching pains in the back, loss of weight, depression and irritability. In August, 1909, he was admitted to the London Hospital complaining of these symptoms, and was found to have a gumma of the left testicle. He was treated with 15 inunctions of mercury, and large doses of potassium iodide, and three weeks later was discharged, free from all subjective manifestations.

He then remained well until August, 1911, when the shivering attacks and feelings of malaise returned.

He was readmitted in April, 1912, and again treated with inunctions of mercury. On admission the temperature oscillated between 100° F. and 101° F. (37·8° C. to 38·4° C.), he complained of shivering attacks and much headache, but the only definite sign discovered was tenderness of the scalp on pressure; and yet on April 3, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$, whilst the cells numbered 112 per cubic millimetre.

After this treatment he remained well until Christmas, 1913; then he began to suffer again from shivering attacks, headache, "rheumatic pains" in the arms, legs and body and somnolence.

On March 2, 1914, he was readmitted with a temperature of 100° F. to 101° F. (37·8° C. to 38·4° C.), which fell after an injection with 0·9 gm. of neo-salvarsan. The mental state, special senses, cranial nerves, motion, reflexes and sphincters were completely unaffected. He complained of headache, which was

accompanied by pressure and percussion tenderness of the skull. Areas of tenderness were found over the outer aspect of the right leg below the knee, along the inner side of right arm and armpit; a band of tenderness was present on both halves of the abdomen below the level of the umbilicus. These areas gave the usual excessive reactions to the dragged point of the pin and to extremes of heat and cold; but no definite loss of sensibility could be discovered.

On March 4, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 117 per cubic millimetre.

He was injected with 0.9 grm. of neosalvarsan on March 5, March 8, and March 11, 1914.

After this treatment the shivering attacks ceased and the areas of tenderness could no longer be determined.

With this case it is well to compare No. 149, p. 58, where the shivering attacks were associated with defective reaction of the pupils and polyuria.

§ 5.—*Root Lesions.*

Neuralgic pains in various parts of the body are recognized as an early symptom of syphilis of the nervous system, but the signs which point to the radicular origin of these pains have not been so generally appreciated.

As soon as a group of muscles begin to waste, the patient consults his doctor; but he does not trouble to complain of a patch of defective sensibility. Yet it is of extreme importance to recognize the significance of these localized sensory symptoms and signs because, in one form or another, they are far commoner than affections of the motor nerve-roots. Moreover, they reveal the changes, occurring within the spinal canal, at a stage when the syphilitic process is amenable to treatment, and has not yet caused irreparable secondary damage.

Our first example is a woman who showed both muscular wasting and loss of sensation in the left lower extremity. The muscles in the upper part of the front of the thigh and the whole of the extensor group were wasted, and there was some loss of power in the flexors and extensors of the left leg.

This muscular wasting was associated with complete loss of sensation to prick, heat and cold over the area shown on fig. 1; the loss of sensibility to cotton-wool was not so clearly defined, and was everywhere somewhat less extensive. This is characteristic of a lesion of the posterior root-fibres, either without or within the spinal cord, before the impulses have undergone regrouping at the first synaptic junction

(Head and Sherren [5]). The sensory loss corresponded to destruction of at least the first and second lumbar roots, whilst the motor disturbance pointed to an even more extensive lesion.

A Case of Disturbance of Motor and Sensory Nerve-roots. Recovery of Power and Disappearance of the Wassermann Reaction in the Cerebrospinal Fluid in consequence of Treatment.

Case 60.—Ada G., female, married; born 1876. This patient was married in 1905 at the age of 29. Shortly after marriage her health failed and eight months later she miscarried of a six and half months' foetus which was peeling; the second child, Jessie G. (No. 61), born in 1906, gives a positive Wassermann reaction in the serum and shows a monoplegia of the right arm; the third

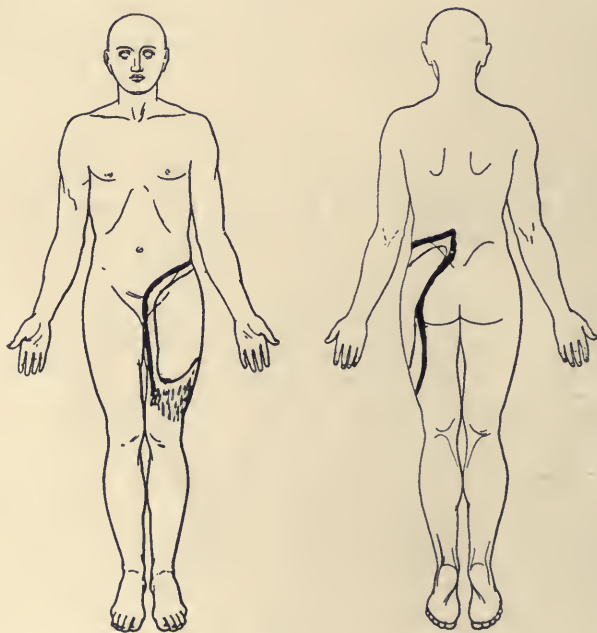


FIG. 1.

child was born in 1907 and is healthy; the fourth was born in 1909. In December, 1909, her husband was admitted to Claybury Asylum, and there, on September 13, 1911, he died; at the autopsy his brain showed the characteristic appearances of "dementia paralytica."

In September, 1910, she began to suffer from pains in the back and down the outer aspect of the left thigh; then the left leg became weak and wasted and her general health again failed.

In July, 1911, she first came under observation. Since this time she has

shown a complete loss of sensibility to painful pressure and the prick of a pin, and to heat and cold, over an area on the front and outer side of the left thigh corresponding to the distribution of the twelfth thoracic and first and second lumbar roots. The anæsthesia to cotton-wool touches was less extensive and the loss less profound (fig. 1). At first the muscles on the front of the left thigh were weak and showed much wasting; there was also paresis and some degree of wasting in the flexor and adductor muscles. The right leg was never affected. The left knee-jerk could not be obtained, and the plantar responses on both sides were flexor.

The patient showed no psychological changes of any kind. Headaches have never been a noteworthy feature and no abnormalities have ever been detected in the territory of the cranial nerves.

On June 25, 1911, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.3.-.-.}$

On June 21, 1911, she was injected intravenously with 0.4 gm. of salvarsan, and this dose was repeated on June 27, 1911.

In June, 1912, the wasting of the left leg, though still considerable, was much less extensive than it had been when she first came under observation. The left knee-jerk had returned and, except for the area of profound loss of sensibility observed in 1911, no signs of nervous disease could be detected.

On June 26, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$

On June 27, 1912, she was injected with 0.6 gm. of salvarsan, and on February 6, 1913, and again on August 2, 1913, she was further treated with doses of 0.9 gm. of neosalvarsan.

Since then no new manifestations of any kind have appeared, and in May, 1914, the sensory loss remained exactly as it was when she first came under observation almost three years previously in spite of the fact that both muscular wasting and loss of motor power had disappeared.

More commonly, however, no muscular wasting can be discovered, and sensory signs and symptoms form the only indication that destructive changes are occurring in the nerve-roots and neighbouring structures. If the pains, of which the patient complains, are associated with areas of partial analgesia and thermo-anæsthesia, together with somewhat less extensive loss of sensation to cotton-wool, the diagnosis is not difficult; it is obvious that the posterior roots are affected, especially if the areas of disturbed sensibility have a radicular distribution.

Sometimes, however, no obvious loss of sensation can be found within the area which reacts excessively to pain and other unpleasant stimuli. By extremely careful examination, we could sometimes discover that within these bands of tenderness pricks of a certain strength seemed "duller" to the patient than over the neighbouring normal parts, although they "hurt" more. But in many cases ordinary

clinical methods do not reveal any definite loss of sensation within those areas which react excessively to painful stimuli. They seem, in such cases, to be simply the results of root-irritation uncomplicated by destruction or secondary degeneration (cf. No. 313, p. 30).

Under such circumstances it is almost impossible to differentiate the effects of root-irritation from the tenderness which accompanies referred pain of visceral origin. It is not difficult to distinguish the pain and tenderness due to root-irritation or to visceral disease from that of a pleurisy or local peritonitis; for the latter usually corresponds to the extent of the inflammation and is accompanied by deep, rather than by superficial tenderness. Moreover, the pain of a pleurisy does not radiate round the body from back to front, and if, as is sometimes the case, superficial tenderness is present it lies in front of the point where friction is audible. For any superficial tenderness which accompanies a pleurisy is due to irritation of branches of the intercostal nerves by the pleural inflammation; consequently it will lie in front of the point at which the pleuritic rub is audible and will not extend back to the spine and round the body like the radicular or segmental areas.

But the differential diagnosis between the tenderness due to root-irritation and to referred visceral pain is not uncommonly so difficult that the abdomen has been needlessly opened in many instances.

In the following case (No. 147) the pain and tenderness were so great that a laparotomy was performed although the Argyll-Robertson pupil should have warned the surgeon of the existence of some disease in the central nervous system. Here we could discover no loss of sensation of any kind; the only change consisted in tenderness over the distribution of the eighth and ninth thoracic roots on both sides of the abdomen.

A Case of Gastric Crises in which the Wassermann Reaction disappeared in the Cerebrospinal Fluid after Treatment with Neosalvarsan, although the Attacks of Vomiting were apparently unaltered.

Case 147.—E. S., male, single, baker; born 1883.

In 1904, at the age of 21, he contracted syphilis and suffered from a "running" followed in turn by a bubo in the right groin, recurrent sore throats and a fall of hair, but no rash. For this he was treated for four weeks only.

In the spring of 1909 after a period of good health he suffered from a severe attack of retching and vomiting. It came on suddenly without any warning and was accompanied by much abdominal pain and tenderness; this first attack lasted four days.

Since this time, at intervals of from four to eight weeks, similar attacks occurred; between them he was perfectly well. They came on without warning and both started and ended suddenly. Of the many drugs tried, morphia only had the slightest effect on the duration of the attacks.

In 1912 laparotomy was performed under the impression that the attacks were due to "gall-stones," but nothing abnormal was discovered in the abdomen.

He first came under observation in May, 1913. At that time he was depressed and his memory was certainly impaired. Speech was unaffected. He had suffered from attacks of apparently causeless vomiting lasting some four to six days accompanied by intense abdominal pain. The attacks whilst he was under our observation were extremely severe. For the last three years at home he had suffered from about one attack in every four weeks, but whilst in Hospital he had four such attacks in seven weeks. In the months preceding admission the severity of the attacks had increased.

He complained of no headache. Vision and the visual fields were unaffected and smell, taste and hearing were normal. The movements of the eyeballs were unbalanced, more especially when looking far outwards to the right and left. The pupils were of pin-point size: in moderate lights the right was larger than the left; neither reacted to light, both reacted on accommodation and convergence. The movements of the face, jaws, palate and tongue were unaffected.

His gait was natural and Romberg's sign was not obtained. The lower extremities were thin, but there was no local wasting of any group of muscles and no hypotonia. Co-ordination of the hands was unaffected.

He complained of spontaneous "rheumatic" pains in the legs; these pains were not associated with any demonstrable changes in the joints. The pain of a prick, heat and cold, two points of the compasses, the situation of a touch, posture, passive movement and the vibrations of the tuning fork were all well recognized on the trunk and extremities. After a gastric crisis tenderness, with hyperalgesia of the eighth and ninth thoracic root-areas, was always present, but three days after each attack these tender areas were no longer demonstrable.

The knee-jerks were obtained on reinforcement and ankle-jerks could be elicited. The plantar responses were sluggish and of the flexor type. The abdominal reflexes and the wrist- and elbow-jerks were unaffected.

At no time had he experienced any difficulty in holding or passing his water or motions.

The movements of the spine were normal.

No abnormal physical signs were found in the heart, lungs, or abdomen. The urine contained neither albumen nor sugar. On the right side of the upper part of the abdomen was a well-healed scar of the laparotomy.

On May 1, 1913, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 4.4.1.0.0.}$ and the cells numbered 12 per cubic millimetre.

He was injected on May 5, 1913, with 0.9 gm. of neosalvarsan and on May 10 and again on May 20 with similar doses; after each injection he suffered from a more or less severe gastric crisis.

No "provocative" Wassermann reaction appeared in the serum; on May 15 and again on May 22, 1913, the Wassermann reaction was serum 0.0.0.0.0.

cs.f. -.-.-.-.

The patient's general health greatly improved under the treatment, but it did not affect the frequency or severity of the gastric crises or the signs by which they were accompanied.

On November 25, 1913, he was readmitted for further treatment and, although the manifestations of the disease were unchanged the Wassermann reaction on November 26, 1913, was serum 0.0.0.0.0.
cs.f. 0.0.0.0.0.

On November 28, 1913, he was treated with 0.9 gm. of neosalvarsan, and again after the injection a gastric crisis developed, lasting on this occasion seven days.

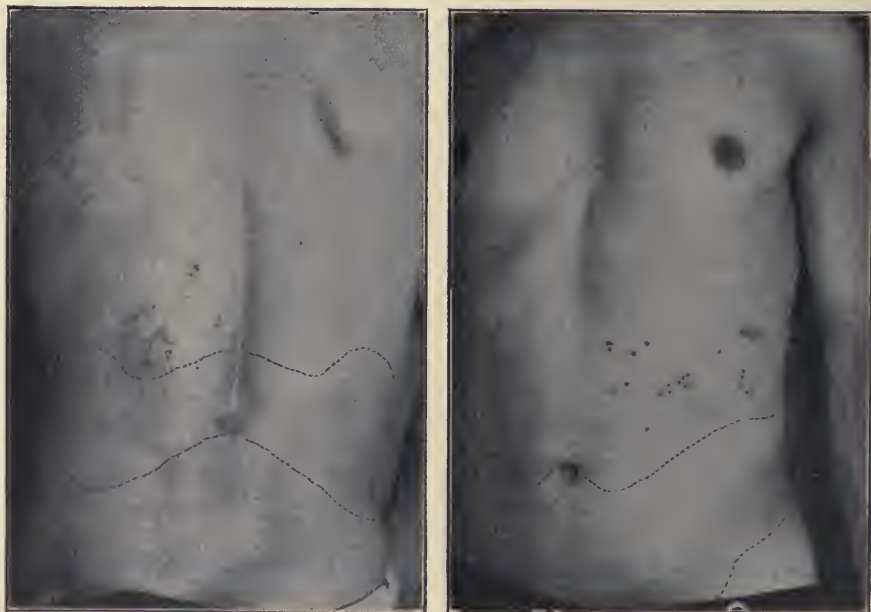


FIG. 2.

Occasionally these root-pains are associated at one time or another in the course of the disease with an outburst of herpes zoster. Thus in No. 125 an attack of zoster appeared over the distribution of the ninth thoracic root on the left side (*vide* fig. 2). This patient had long suffered from a girdle sensation, accompanied by tenderness over

the extent of the tenth and eleventh thoracic areas on both halves of the body. Thus the herpetic eruption on the left side revealed the spread of the meningeal inflammation to the next root above the level of the previous irritative lesions. (For a full account of this case *vide* p. 130.) Similarly in No. 91 the patient had long suffered with pains and excessive reaction to disagreeable stimuli over the distribution of the eighth and ninth thoracic roots on both sides; suddenly he developed pains of a similar character in the left half of the neck, followed by a characteristic herpetic eruption over the second cervical root-area. (For a full account of this case, *vide* p. 73.)

So common are these root lesions in cerebrospinal syphilis, that we look upon them as a most valuable early sign that the structures within the spinal canal have been attacked (cf. No. 313, p. 30). They not infrequently occur in cases where the principal manifestations point to some cerebral lesion, and they are then, as a rule, overlooked. But whatever the other signs and symptoms may be, these areas of pain and tenderness point to affection of the spinal roots and so indirectly to meningeal inflammation; and the occurrence of the changes of the spinal meninges are a significant factor in the interpretation of the results yielded by the Wassermann reaction. Thus these radicular areas of tenderness are of extreme importance, not only in diagnosis and as a guide to early treatment, but also in determining the meaning of the Wassermann reaction in the cerebrospinal fluid.

§ 6.—*Abnormal Reactions of the Pupil.*

Some abnormality in the reaction of the pupils occurs in a large number of cases of syphilis of the central nervous system, apart altogether from tabes dorsalis and dementia paralytica. We have excluded from consideration in this section these two conditions, and also all cases of congenital syphilis; for in-patients who are the subjects of congenital syphilis, changes in the iris, consequent on keratitis punctata and iridocyclitis, frequently make it impossible to test the reactions of the pupils. We were then left with sixty-eight cases of cerebrospinal syphilis; but in five of these patients the iris was fixed to a greater or less extent by adhesions the result of old inflammation, and they were therefore excluded.

Out of sixty-three cases, 33 or 50 per cent. showed some abnormality of reaction in one or both pupils. Of these eleven were totally inactive to light, whilst in the remainder the reaction occurred, but was not

maintained, or the contraction was slight and required an intense light before it was evoked. Occasionally the pupils were badly centred and they were frequently of unequal size; these, however, we have not included amongst the thirty-three abnormal cases, unless they also showed some slowness or other defect of reaction.

If we consider the eleven cases only where the pupils were inactive to light, our experience corresponds fairly well to that of other observers; Uhthoff [22] found ten cases in 100 patients with cerebral syphilis and Nonne ([13], p. 211) states that slighter abnormalities are not uncommon.

We believe that abnormal pupillary reactions are a most valuable sign of infection of the nervous system, especially where the other manifestations are of doubtful significance. In cases of pain and tenderness in the abdomen or chest without signs of visceral disease, or where the symptoms point to neurasthenia the presence of some defect in the reaction of the pupils will clinch the diagnosis in favour of syphilis of the central nervous system (*vide* No. 147, p. 22).

Aortic disease of syphilitic origin is sometimes accompanied by infection of the central nervous system. Thus in one case of this kind (No. 171) the sluggish reaction of unequal excentric pupils was the only sign that the central nervous system was affected.

According to our experience some disturbance of the size, shape or reaction of the pupils to light forms a frequent and an early sign of syphilitic disease of the central nervous system. Abnormal reactions of the pupil are in no way confined to tabes dorsalis and dementia paralytica, but occurred to a greater or less extent in one half of our cases of cerebrospinal syphilis.

§ 7.—*Disturbances of Micturition.*

It is not uncommon, in cases of syphilis of the nervous system, for some disturbance of micturition to be the first cause of the patient's consulting a doctor. But our opportunities of observing this symptom are not so great as with the other conditions described in this section; for a man suffering with some difficulty in micturition will go to a surgeon rather than to a physician. As soon as he is found to be a case of cerebrospinal syphilis, he is treated by the surgeon and does not come under our observation. Our material is not, therefore, a fair sample for determining the frequency with which some defect in micturition forms the initial symptom in cases of cerebrospinal syphilis.

It is, however, well recognized (Nonne ([13], p. 380) that, when syphilis attacks the spinal cord, some difficulty in micturition is usually one of the earliest symptoms. This was so in No. 19, chosen to illustrate this point because the Wassermann reaction in the cerebrospinal fluid rapidly became negative after treatment. Another instance where bladder symptoms appeared as the initial manifestation is No. 125 (see p. 130), a case of combined meningo-vascular and central syphilis.

A Case of "Meningomyelitis" which started with Bladder Symptoms. The Wassermann Reaction, at first strongly Positive, became and remained Negative in the Cerebrospinal Fluid in consequence of Treatment.

Case 19.—D. B., male, married, grocer; born 1870. In 1890, at the age of 20, this patient contracted a "running," but did not suffer from a sore or any manifestations of secondary syphilis. He was not treated, but remained in good health until 1907; he then developed retention of urine with cystitis and was in bed six weeks.

In February, 1912, after fourteen days of malaise and general pains, he again developed urinary trouble accompanied by pain in the back and abdomen. Whilst he was in bed he developed weakness and stiffness of the right leg. During the month of April, 1912, he seemed to improve, but on May 15, 1912, the left leg became affected and the abdominal pains returned. From that time until his admission on August 1, 1912, he became gradually and progressively worse.

On August 1, 1912, his mental state was unaffected and his speech was natural. He had suffered from no headache, no seizures and no attacks of vomiting. The cranial nerves and fundi were unaffected.

The left hand was unsteady and clumsy in action and the alignment of the fingers was bad. The left leg was completely paralysed and there was grave weakness of the right leg, so that movements could not be performed against slight resistance. The muscles of the lower extremities and of the abdomen, together with the lower portion of the erector spinæ on both sides, showed severe wasting and flaccidity.

He complained of spontaneous pains about the region of the nipples on both sides, and the areas supplied by the third to the sixth thoracic roots were tender to the dragged point of a pin. Below this zone all forms of sensibility were gravely impaired; on the left leg the impairment was greatest to passive movement, posture, the vibrations of a tuning-fork, and the compass-test. On the right leg the loss of sensation was greatest to painful stimuli and to the thermal tests.

Both knee-jerks were much exaggerated, the left more so than the right. Ankle-clonus was readily elicited on both sides, and both plantar reflexes gave an extensor response. The abdominal reflexes could not be obtained.

He could not pass his urine and there was incontinence from overflow, with inability to hold the motions when soft.

On August 2, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.3.2.}$

He was given 0.6 gm. of salvarsan on August 1, 1912, followed by 0.9 gm. of neosalvarsan on August 6, 1912.

On September 2, 1912, he was discharged from hospital able to walk. The wasting of the legs and of the abdominal and erector spinæ muscles after the injections diminished considerably under treatment with massage.

He returned for further treatment on May 19, 1913. At that time the left pupil reacted sluggishly to light whilst the right reacted briskly; otherwise nothing abnormal was discovered in the territory of the cranial nerves. The left leg was smaller in circumference than the right; both legs were spastic and there was obvious ataxy of the left leg on walking. Sensation was impaired on both sides below the level of the umbilicus and the patient still experienced trouble in holding and passing water.

On May 21, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 4 per cubic millimetre. On the same day he was given another dose of 0.9 gm. of neosalvarsan.

When reinvestigated on February 18, 1914, the nervous condition had not changed from that seen in the previous May, and the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

CHAPTER IV.—SYPHILIS MENINGO-VASCULARIS.

This group of syphilitic affections of the central nervous system includes most of the conditions usually spoken of as "subacute," "chronic," "tertiary," and "gummatous." Pathologically they are known to depend, for the most part, on disease of the meninges and vessels. But from clinical evidence alone we can recognize, in many cases, that the signs and symptoms point mainly to affection of meninges and vessels. Thus paralysis and irritation of spinal roots are produced in the majority of cases by meningitis, whilst hemiplegia and the condition usually attributed to "encephalitis" are due largely to vascular occlusion or to the rupture of weakened vessels. We do not require a *post-mortem* examination to recognize that, whatever other lesions may be present, these cases depend for their clinical manifestations on changes in the meninges and vessels.

Now, wherever symptoms and signs point to meningeal and vascular lesions, they are found to be peculiarly amenable to anti-syphilitic remedies. Not only is the disease affected favourably, but the Wassermann reaction, if positive in the cerebrospinal fluid, may become negative within a few months after treatment. At the same time

the excess of cells in the cerebrospinal fluid may become greatly reduced.

But though clinical and serological examination may indicate that any particular case belongs to the meningo-vascular group, we do not believe that a series of patients can be separated into two sharply defined and naturally exclusive classes, those with syphilis meningo-vascularis and those with syphilis centralis. For in most cases there is no essential pathological difference between them; the two conditions are the expression of a similar process acting in two different situations upon different anatomical structures. These anatomical differences lead to a diversity both in the clinical manifestations and therapeutic behaviour. Many cases, as it happens, show no signs of primary destruction other than that in the meninges and vessels; but in some instances the course of the disease and the behaviour of the Wassermann reaction under treatment betray the existence of additional foci of morbid activity deep in the structures of the central nervous system. Such cases are classed by us as "mixed forms," and will be considered in Chapter VI.

In the present chapter we shall deal with those varieties of cerebrospinal syphilis, in which the signs and symptoms, the behaviour of the Wassermann reaction, and the pleocytosis, point to some affection of the meninges and blood-vessels.

Not uncommonly the clinical phenomena of meningo-vascular syphilis are described as "secondary" or "tertiary" manifestations; in some cases a diagnosis of "diffuse gummatosis" is made at the bedside because the first symptoms appeared many years after infection; whilst a similar clinical condition, occurring during the first year, is attributed to secondary syphilis.

We wish to insist on the view that the nature of the clinical manifestations of meningo-vascular syphilis at their first onset does not differ materially according to the period which has elapsed since the disease was acquired. They express the disturbances of structure and function caused by the inflammatory reaction in the central nervous system, and not the stages of syphilitic infection; irritation of posterior roots, cranial nerve paralyses, hemiplegia of vascular origin, will not differ clinically according to the stages of syphilis, but will depend on the extent of the inflammatory reaction and the nature of the structures affected.

Thus the following patient (No. 313) showed signs of profound irritation of many spinal nerve-roots three months after infection,

accompanied by a copious lenticular syphilide, mucous patches, condylomata, and general adenitis. The pyrexia and other signs of secondary syphilis disappeared under treatment with neosalvarsan, and five days after the first injection no abnormal nervous manifestations could be discovered. The cerebrospinal fluid gave a positive reaction, and contained a large excess of polymorphonuclear cells.

A Case of Secondary Syphilis, within Three Months of Infection, where the signs of Irritation of many Nerve-roots were accompanied by a positive Wassermann Reaction in the Cerebrospinal Fluid and great Pleocytosis.

Case 313.—C. G., female, married; born 1878. This patient was infected with syphilis by her husband early in March, 1914, when six months pregnant with her eighth child. At the date of infection her husband was apparently healthy; subsequently, however, during the months of April and May, he suffered from a series of bad throats, accompanied by malaise, irritability, and pains in the head, trunk, and extremities, but no rash. Towards the end of March, 1914, the patient noticed a more copious vaginal discharge than with any of her other pregnancies, and a few weeks later discovered a sore on her vulva. Early in April she began to suffer from a tired feeling and aching in her lower extremities; then a ham-coloured rash appeared on her abdomen, and subsequently affected almost the whole of the skin of the body. Condylomata appeared around her vulva and anus, followed, about May 17, by the development of a sore throat. After the first week in May she became unable to do her work owing to a severe, dull pain in the head, accompanied by a feeling of sleepiness during the day, with restlessness and inability to sleep by night. Two weeks later she suffered from pains shooting down the inner side of her arms, and down the back of the legs, together with a tight feeling in the lower abdomen and back. About the middle of April, 1914, she sought the advice of her local doctor; the rash was diagnosed as syphilitic and she was treated with mercury by the mouth. In spite of this treatment, however, the rash continued to develop and new manifestations appeared almost daily, until her admission to the London Hospital on June 3, 1914, under the care of Dr. J. H. Sequeira.

On admission, there was a copious lenticular syphilitic rash, widely distributed all over the face, trunk and extremities. The left labium majus was swollen and cedematous. Condylomata were present around the vulva and anus, and there was hyperkeratosis of the soles of both feet. The glands of the groins, at the elbows and on both sides of the neck were enlarged, hard and shotty. She complained of a sore throat, and mucous patches were observed on both tonsils. The temperature was raised and ranged from 98° F. to 101° F. (36·7° C. to 38·4° C.). The rate of the pulse varied from 96 to 120 beats per minute. There was no cardiac enlargement, but the sounds were indistinct and distant. No abnormal signs were detected in the lungs, or in the abdomen, which contained an eight months' pregnant uterus. The urine contained a trace of albumen, but no pus and no sugar.

Mentally she was depressed and worried. She said that for six weeks she had been subject to attacks of crying; she would weep copiously for ten minutes, without any apparent cause, and then stop, "feeling herself again." Mentation was slow, but her memory was little impaired. She felt sleepy, but slept badly and was restless by night. Attention and speech were unaffected. She had suffered from no seizures or attacks of vomiting. Hallucinations and delusions were not present and she had not been troubled by dreams or nightmares.

The special senses were unaffected and the movements of the eyes, pupils, jaws, palate, larynx and tongue were normal. Motion was unaffected, her gait was normal and the grasps of the hands powerful.

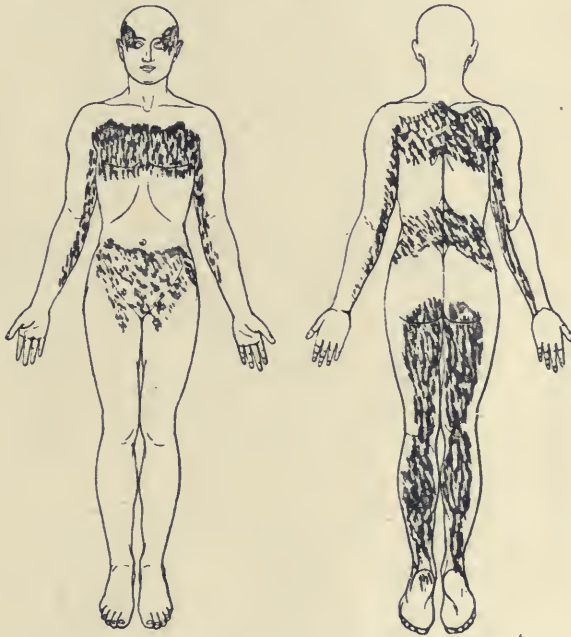


FIG. 3.

She complained of (1) an intense headache with shooting "neuralgic" pains in the temples; (2) of tenderness and shooting pains in the upper part of the chest and along the inner aspect of the axillæ, arms and forearms on both sides: (3) tightness and uncomfortable sensations in the lower part of her abdomen and the upper part of both thighs; (4) shooting, gnawing pains in the backs of the thighs and calves. These pains were aggravated by movement and relieved by rest in bed. Over the areas where the patient complained of pain, the skin was tender and responded excessively to the dragged point of a pin, to pinching and to pressure (fig. 3). She said that these stimuli "felt different," but no sensory loss of any kind could be detected. These

areas corresponded to the peripheral distribution of the second, third, fourth, eleventh, and twelfth thoracic, and the second and third sacral nerve-roots, and to a portion of the distribution of the ophthalmic division of the trigeminal nerves.

With the exception that the right plantar reflex gave an indefinite extension, whilst the left was definitely flexor, all the reflexes were completely unaffected.

She was constipated and had never complained of any difficulty in controlling her motions; but she said that she had found great difficulty in holding and in passing her water, and had at times wetted herself.

The cerebrospinal fluid was collected on June 5, 1914, twenty-four hours after she had been injected with a dose of 0.45 gm. of neosalvarsan, and was tested on June 10, 1914, when the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.0.0.0.}$

On June 5, the cells in this fluid numbered 153 per cubic millimetre; of these cells 75 per cent. were polymorphonuclear, and 3 per cent. plasma cells, and the rest were lymphocytes.

On June 6, 1914, she was further injected with 0.9 gm. of neosalvarsan and this dose was repeated on June 8.

The temperature fell to normal before the second injection was given on the 6th; after this injection she said she felt "much better," the pains ceased and the rash began to disappear. On the 7th the areas of tenderness were no longer definite, and on the 9th they could not be discovered; at the same time the rate of the pulse fell to 72 beats per minute, the patient became cheerful and her mentation improved to a remarkable extent. On June 10, when she was discharged, the rash had almost completely faded, the glandular enlargement was no longer evident, and no abnormal nervous manifestations of any kind could be discovered.

Not only may signs of irritation of spinal nerve-roots make their appearance shortly after infection, but a condition may arise accompanied by signs of gross disease indistinguishable from those frequently seen in the later stages of the disease. Thus, for instance, No. 309, within three months of infection, showed signs of paralysis of many cranial nerves, irritation of the trigeminal, the third, eleventh, and twelfth dorsal, and second and third sacral roots, together with slight difficulty in micturition, a clinical condition exactly comparable to that discovered in No. 3, where the first manifestations of affection of the nervous system did not appear until twenty-three years after infection.

Widespread Signs of Cerebrospinal Syphilis within Three Months of Infection.

Case 309.—J. W., male, single, stoker; born 1876. In October, 1913, at the age of 37, he contracted syphilis and developed a chancre. On November 4, 1913, he was admitted to the Seamen's Hospital, Greenwich,

with a chancre and a rash which were treated with an intravenous injection of neosalvarsan and black wash. Under treatment the chancre healed and the rash disappeared, and he was discharged feeling well on December 1, 1913.

About three weeks later he began to complain of "pains all over," in the shoulders, knees, wrists, feet and lower abdomen, and intense, throbbing "headaches."

Early in January, 1914, the right side of his face became paralysed, and a few days later he found that he could not walk straight.

On February 10, 1914, he first attended the dermatological clinic of the London Hospital, where he was treated with mercury by the mouth, and on April 5, 1914, he was admitted to Hospital under the care of Dr. J. H. Sequeira.

On admission he was found to be an extremely powerful, well-developed man. He was stone deaf and all communications with him had to be carried on by means of writing. He said that this deafness had come on after an attack of pneumonia at the age of 5, and that in recent times it had not increased. He answered written questions readily and lucidly. He was attentive and gave his history in clear and logical sentences. The drums of both ears showed scars of old perforations. On the prepuce was a scar of an almost completely healed chancre. No rash was present and there was no glandular enlargement. The temperature was not raised; the rate of the pulse was 72 beats per minute.

He complained of severe, grinding and throbbing pains in the head: they were constant and were worst along the base of the skull, in the frontal, temporal and occipital regions. These pains were intensified on pressure. He had not suffered from any seizures or attacks of vomiting and, in spite of the deafness, speech was unaffected. He complained that the sight of the right eye was misty, but the optic discs and fundi appeared healthy. Smell and taste were unaffected. He complained of diplopia and squinted with the right eye. The external rectus muscle on the right side was almost completely paralysed, and all the muscles moving the right eye-ball were paretic. The pupils were well centred, equal and reacted normally to light and accommodation. The muscles moving the right half of the jaw were weak; the masseter on this side contracted feebly and the angle of the jaw swung to the left when the mouth was opened widely. He complained of spontaneous pains along the peripheral distribution of the second division of the right trigeminal and, over an area bounded by the upper margin of the malar bone, the ear, and the lower margin of the mandible, the skin was tender and reacted excessively to the dragged point of a pin. The exact sensory interference over this area could not be determined owing to the deafness of the patient. The upper and lower halves of the face on the right side were almost completely paralysed. The right half of the palate moved badly and the uvula swung to the left on phonation. The sternomastoid and trapezius muscles on both sides were well developed. The tongue was protruded straight and was held steadily. All his movements were clumsy and unsteady. The gait was rolling. Romberg's sign was not present.

The grips were powerful. There was no local muscular atrophy and no spasticity.

He complained of spontaneous pains: (1) in the right upper jaw; (2) in the right axilla and in the upper part of the right arm; (3) in the lower abdomen and back on both sides, "a sort of constriction with darting stabs" greater on the left side than on the right; (4) in the back of both thighs and down the calves, more severe and more constant on the left side than on the right. The areas over which the patient complained of spontaneous pains responded excessively to the dragged point of a pin, and corresponded with the peripheral distribution of the second division of the right trigeminal nerve, the right third thoracic nerve-root, the eleventh and twelfth thoracic nerve-roots, and the second and third sacral roots on both sides. Owing to the deafness of the patient a more detailed examination was impossible. The vibrations of a tuning-fork were well recognized everywhere.

The left knee-jerk was greater than the right but both were readily obtained. The ankle-jerks on both sides were brisk. The plantar reflexes were difficult to obtain and were doubtfully extensor in character. The abdominal reflexes were unaffected. The right wrist- and elbow-jerks were exaggerated as compared with those of the left side. At times he had suffered from some hesitation in passing urine, but whilst in bed he had no difficulty in controlling either the rectum or the bladder.

On April 15, 1914, the Wassermann reaction was $\frac{\text{serum } 4.}{\text{cs.f. } 4.4.4.0.0}$ and the cells numbered 42 per cubic millimetre. He was treated with injections of 0.9 gm. of neosalvarsan on April 6, and on April 8, 1914, followed by eight intramuscular injections of mercury cream. On July 15, 1914, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 2.0.0.0.0.}$ and the cells numbered 17 per cubic millimetre.

Affection of many Cranial Nerves and of the Optic Tract arising Twenty-three Years after Infection. Syphilitic Psychosis. Root Lesions. A strongly Positive Wassermann Reaction in the Cerebrospinal Fluid, which became Negative under Treatment.

Case 3.—A. A., male, married, commercial traveller; born 1864. In 1888, at the age of 24, whilst serving in the Army, this patient caught syphilis; he developed a chancre, which healed under a course of mercury lasting a few weeks only, and was not followed by any rash or sore throat.

From his discharge from the Army in 1892 until 1910 he lived the life of a commercial traveller, taking a considerable amount of alcohol, but on the whole remained in good health.

During the year 1911, he suffered from lassitude and chronic headaches. His memory gradually became bad, and his mental powers decreased. Early in 1912 he had to give up all work, and could not even look after a golf club-house of which he had been appointed caretaker.

He cannot remember what happened to him during the months between March, 1912, and February, 1913; he went from hospital to hospital, but under out-patient treatment gradually grew worse.

In February, 1913, he first experienced diplopia; then for the first time pains became troublesome, and he gradually developed difficulty in holding and passing water.

On April 24, 1913, he was admitted to the London Hospital. At that time he was dull and stupid. He answered questions slowly, but reasonably and correctly. In general conversation his remarks were inconsequent. He gave his history in a rambling manner, and his memory showed enormous blanks when he attempted to recall the events of recent years; it was particularly defective with regard to everyday matters of common knowledge, such as the day on which people usually go to church. He was inattentive, but contented and not over emotional. He slept very heavily, and for the greater part of the twenty-four hours he was drowsy or asleep. He complained of dreadful nightmares and day dreams. He said that he seemed to be always going over his Indian experiences and to be "fighting in odd corners of the globe against fearful odds." "At night, lions and bears seem to be crawling about me," and by day he would misinterpret objects in the wards in terms of his dreams.

Speech was slurred and gabbled, words and syllables being frequently missed out. He had not suffered from seizures, attacks of vomiting or retching.

He complained of severe grinding and gnawing headaches over the vertex and along the base of the skull; the whole scalp was extremely sensitive to pressure.

Both visual fields were much diminished; on the left side the temporal field was almost completely abolished and on the right the nasal half of the field was small, whilst central vision was much impaired. The fields had the same form and outline for all colours. Both optic discs and the vessels of the fundi appeared natural.

Hearing with both ears was unaffected, but taste was much impaired and smell completely abolished.

The right eyelid drooped. The eye movements were unbalanced, and the axes of the eyes rarely moved together; downward movements of the right eye were impaired, and in consequence the patient complained of diplopia (paresis of right third cranial nerve).

The right pupil was dilated, the left small; both were ovoid in outline, and their margins irregular; they reacted extremely sluggishly to light and to accommodation.

The muscles moving the right half of the jaw were paretic and dissociated anæsthesia was present on the right cheek, forehead and anterior portion of the scalp; sensibility to pain, heat and cold was lost over this area whilst that to light touches of cotton-wool was retained. The right cornea was anæsthetic.

The right facial muscles were paretic in movement and at rest showed

overaction. The palate on phonation was drawn to the left, the right half being immobile.

The movements of the larynx were well carried out and swallowing was not affected. On the right side the sternomastoid and trapezius muscles were wasted and there was difficulty in rotating the head.

The tongue was protruded slightly towards the left; fibrillary tremors and wasting were not observed.

The gait was unsteady and clumsy. Romberg's sign was not present. The balance of the fingers was bad and co-ordination of the hands was defective; closure of the eyes did not increase this inco-ordination of the hands. The muscles of the left thigh, more especially those of the extensor group, were wasted. The left buttock was well developed, and the calf muscles appeared natural.

He complained of spontaneous pains in the chest, abdomen and legs, and areas of tenderness, with some loss of sensibility, were present over the distribution of the third and sixth thoracic roots and the third lumbar roots on both sides. Posture and passive movement were well appreciated on the legs and the replies to the tuning-fork tests were accurate everywhere.

The knee-jerks on both sides were exaggerated; ankle-clonus was readily elicited on the right side, but could not be obtained on the left. The abdominal reflexes were absent. Both plantar reflexes gave an extensor response. The right corneal reflex was not obtained, but on the left side it was normal.

The patient complained of difficulty in holding and passing his water, and he not infrequently wetted himself; occasionally also, he was unable to control his motions especially when they were soft.

The spine was straight and moved naturally. No abnormal signs were discovered in the heart, lungs or abdomen and the urine contained neither albumen nor sugar.

On April 30, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.3.2.}$ and the cells numbered 30 per cubic millimetre.

He was given 0.9 gm. of neosalvarsan on May 1, 1913, on May 9, 1913, and on June 26, 1913.

After this treatment on October 29, 1913, the Wassermann reaction became $\frac{\text{serum } 4.4.4.4.1.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 4 per cubic millimetre.

Soon after treatment was begun his mental condition improved enormously; the paresis of the right third, fifth and seventh cranial nerves became less obvious; the wasting of the muscles supplied by the right spinal accessory nerve and that of the left thigh became less noticeable; whilst the spontaneous pains in the limbs and trunk ceased, the areas of tenderness disappeared, and the headache became no longer troublesome. Between April and October, 1913, the patient gained 12 lb. ($5\frac{1}{2}$ kg.) in weight.

We have shown that the clinical manifestations of cerebrospinal syphilis do not differ in the various "stages" of infection; in the same

way the pleocytosis and the behaviour of the Wassermann reaction in the cerebrospinal fluid form no guide to the period that has elapsed since the patient was infected. Thus, No. 59, within ten months after infection, yielded a highly positive Wassermann reaction in the cerebrospinal fluid, which rapidly became negative under treatment.

A Case of so-called "Syphilitic Encephalitis" arising within Seven Months of Infection where a highly Positive Wassermann Reaction both in Serum and Cerebrospinal Fluid became Negative within Six Months of Treatment.

Case 59.—J. G., male, single, railway fireman; born in 1886. This patient contracted syphilis about Christmas time, 1911, aged 25. He developed a sore, for which he attended the Lock Hospital and was circumcized. Shortly after this a rash and sore throat developed. He received injections of mercury whilst an in-patient, and then took mercurial pills regularly from January, 1912, until July, 1912.

In July, 1912, his memory failed and he lost his job "because he was too sleepy and was found asleep on his engine." In the following month, about August 26, he first complained of abdominal pains and general malaise. Fourteen days later he became stuporose and sleepy; for some days he refused to answer questions, speech became affected and then paresis of the left half of the face and of the right hand developed and he passed his water under him. Seven days later he seemed to improve and was able to go about again.

On the morning of October 3, 1912, on waking after a restless night he found that he could not move his legs nor pass his water, and on that day for the first time he passed a motion into the bed.

On October 7, 1912, he was admitted to Hospital under the care of Dr. Robert Hutchison. He complained that he felt "cold," and that his memory was a bit "off," that he felt "tired" and that he did not want to "budge." Cerebration was slow; he repeated orders and sentences addressed to him and eventually attempted to carry them out. Attention was feeble and fleeting. Speech was little affected. When left alone he was drowsy and somnolent and took no interest in the events of the ward. Delusions were not present.

Hearing, smell and taste were unaffected and the optic discs and fundi appeared natural.

The ocular movements were well carried out and ptosis was not present. The pupils were of normal size and reacted well to light and on accommodation. The left side of the face was flattened and appeared paretic on movement; tremor of the lips was observed on both sides. The motor and sensory fifth cranial nerves were unaffected. Movements of the palate, larynx and of deglutition were natural. The tongue showed coarse tremors.

All movements of the upper extremities could be carried out at will in an ineffective, clumsy, unsteady manner. The outstretched hands were held in the posture of weakness with the fingers out of alignment. Both feet were

dropped, the left more noticeably than the right. The muscles of the legs were flabby but not wasted. He was unable to lift his left leg from the bed and could lift the right leg with difficulty only. Rotation of the right hip was relatively powerfully performed and flexion of the right knee was just possible. The lower abdominal muscles were paretic on both sides.

He complained of spontaneous pains in the legs. The calf-muscles were exquisitely tender to pressure, and he resented pressure applied to any of the paretic muscles. Touch, pressure, heat, cold and passive movements were well recognized both from upper and lower extremities. Areas of tenderness showing hyperalgesia to the dragged point of a pin were present on the lower abdomen and back, apparently corresponding with the distribution of the eleventh and twelfth thoracic roots on both sides.

Both knee-jerks were obtained; ankle-clonus was not present and the ankle-jerks were not elicited. The plantar reflex on both sides gave a flexor response. The lower abdominal reflexes could not be obtained, the upper ones were readily elicited. Kernig's test was positive with both legs.

The skin was moist, dirty, oily and had a nauseous odour. The knee-joints on each side contained an excess of fluid.

He was unable to control his sphincters and passed urine and fæces incontinently into the bed. The spine was straight and its movements unaffected.

He was a well-built, well-developed man, weighing 11 st. 10 lbs. (74½ kg.).

The temperature on admission and until treatment was applied was raised to about 100° F. (37·8° C.) and the rate of the pulse varied from 90 to 100 beats per minute.

The vessels were not thickened. There was no cardiac enlargement, but the sounds were shortened and the rhythm tic-tac; no murmurs were present.

He was treated with injections of neosalvarsan, receiving 0·9 grm. intravenously on October 14, October 21, November 4, December 11, 1912, and on March 6, and April 23, 1913.

Under treatment he improved rapidly, and on November 9, 1912, walked out of Hospital. By April, 1913, all the physical signs of gross nervous disease had disappeared, but mentally he was more feeble than formerly and could no longer "think or be trusted." Since this time his condition has remained stationary.

The Wassermann reaction was :—

On October 8, 1912, $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.3.}$ On October 30, 1912, $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.1.0.}$ and the cells numbered 16 per cubic millimetre. On December 10, 1912, $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 4.4.3.0.0.}$ On March 5, 1913, $\frac{\text{serum } 4.4.1.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 4 per cubic millimetre. On April 23, 1913, $\frac{\text{serum } 1.0.0.0.0.}{\text{cs.f. } \dots\dots\dots}$ On October 29, 1913, $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } \dots\dots\dots}$ On April, 23, 1914, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

[A] CLINICAL VARIETIES.

Fortunately no one has attempted to divide the manifestations of cerebrospinal syphilis into separate "diseases," as has happened with "parasyphilis." We speak of syphilitic "encephalitis," "myelitis," "hemiplegia," "muscular atrophy," "combined sclerosis," and give to each case some name illustrative of its principal signs and symptoms. But it is universally recognized that closer observation will usually reveal additional signs of the activity of the virus in some distant part of the central nervous system. One of the most striking characteristics of the activity of meningo-vascular syphilis is the frequency of multiple lesions; in most other diseases of the nervous system we attempt to postulate one lesion to account for all the signs and symptoms, whilst evidence of multiple syphilitic foci is the rule rather than the exception.

Thus hemianopia may be associated with disturbance of the third, fifth, and seventh cranial nerves, and at the same time the sphincters may be affected (No. 3, p. 34). Paralysis of the cranial nerves and optic neuritis may be accompanied by affection of thoracic nerve-roots and of the sphincters (No. 94); in this case a gumma of the scalp betrayed the nature of the lesions in the central nervous system. Cases apparently of pure "myelitis," such as No. 175, may be complicated by abnormal reactions of the pupils. In No. 59 (p. 37) the changes in the nervous system were so widespread, ten months after infection, that the patient showed alteration in speech, affection of the motor and sensory nerve-roots on the trunk, and loss of control over the sphincters.

When a disease assumes such infinite forms it is useless to attempt to separate its manifestations into "types"; each case reveals a distinct combination of signs and symptoms. But for clinical purposes cases may be grouped roughly according to the situation of the principal lesions, and we shall now give some examples of the forms which can be assumed by syphilis meningo-vascularis, indicating at the same time the behaviour of the Wassermann reaction.

§ 1.—*Cerebral Forms.*

Gross cerebral symptoms, consisting of hebetude and more or less severe loss of memory, amounting in some cases to acute dementia, may appear at any time from a few months to twenty years or more after infection. This so-called syphilitic "encephalitis" or "meningo-encephalitis" is universally recognized to depend on inflammatory changes in the membranes, with endarteritis of the vessels of the brain followed by a varying amount of secondary atrophy and sclerosis.

A Case of Syphilitic Dementia. The Cerebrospinal Fluid gave a negative Wassermann Reaction throughout.

Case 53.—R. F., male, single; born 1880.

He was of good birth, but in 1901 became bankrupt and went to South Africa as a trooper. In 1904 he was in England, in excellent health, but then began to wander again and finally went to Canada. He probably became infected with syphilis about this time. In 1909 and 1910 he worked on a tramp steamer and was admitted to the London Hospital in March, 1912. On admission he lay curled up in bed and never spoke unless he was questioned. He then answered sensibly, but his memory was extremely bad and his attention feeble. He had no conception of time and space and did not know his age or where he was.

He complained of no headache and, as far as his relatives knew, had had no fits or other attacks. He vomited occasionally.

The hands were tremulous, but there was no paralysis, weakness or rigidity anywhere. All movements could be executed well.

No loss of sensation was discovered, as far as he could be tested, and he could recognize the position of his limbs after they had been moved passively.

Knee- and ankle-jerks were brisk; there was no ankle-clonus and both plantar reflexes gave a flexor response.

On ophthalmoscopic examination the vessels of the right disc were seen to be congested and the cup somewhat filled in, but the edges were clear. The left disc was normal.

The pupils reacted well and were equal and regular in outline. There was no ocular paralysis or nystagmus and the movements of the face, tongue and palate were normal.

He gave no indication that he wanted to pass water or evacuate his bowels: thus, unless he was made to micturate at regular intervals, he passed both urine and fæces into the bed. This was, however, due to mental hebetude, and not to true incontinence of urine.

On April 24, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells in cerebrospinal fluid were 2 per cubic millimetre.

In May and June he was treated with mercurial inunctions and on July 7, 1912, he received 0.6 gm. of salvarsan intravenously.

On June 5, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f. } 0.0.0.0.0.}$

He was readmitted on October 15, 1912, greatly improved. He now talked spontaneously and answered questions readily. He had no recollection of his previous stay in the London Hospital. He read for amusement and wrote well to dictation, many of his old interests had returned and he played golf all day.

His speech was monotonous and face rather expressionless, but otherwise his physical state was unchanged. He had complete control of his sphincters.

On October 16, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

On October 16, 1912, he was given 0.9 grm. of neosalvarsan intravenously.

By October, 1913, he had still further improved. He had reduced his golf handicap to four, and still led an absolutely idle life. On October 29, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and there was 1 cell per cubic millimetre.

This is a characteristic instance of the effects of syphilis meningo-vascularis in a young man and, although he improved greatly under treatment, he remained, like so many of these patients, without moral energy or a desire to work. Such an after-result is not, however, always entirely due to the disease; most of these young men were inherently untrustworthy in money matters, and disinclined to an orderly life before any signs of nervous disease appeared. To this rule No. 53 was no exception.

Occasionally this form of cerebral syphilis evokes in young men a condition indistinguishable at first sight from dementia præcox. The inhibition of mental processes, want of emotional expression, and negativism, that go to form the characteristic picture of this disease, may be present, but the increased cell-content of the cerebrospinal fluid and the remarkable improvement under anti-syphilitic remedies show that it belongs to the acute syphilitic dementias.

Our second instance is a man, aged 42 (No. 271), in whom acute stupor, followed by dementia, arose twenty years after infection.

Acute Syphilitic Dementia arising Twenty Years after Infection. Wassermann Reaction Negative in the Cerebrospinal Fluid; Great Pleocytosis.

Case 271.—A. M., male, married, foreman in chemical works; born 1872.

In 1894, at the age of 22, he contracted syphilis and suffered from a sore, for which he was treated for six weeks. No manifestations of secondary syphilis developed, and he remained in good health.

He married for the first time in 1898, and two healthy children of this marriage survive. In 1904 he married for the second time; by this wife he has two living children, and a third died of "weakness and wasting" at the age of three weeks.

In 1909, at the age of 37, his general health failed and he developed leucoplakia of the tongue; since then he has never been well. About Christmas, 1912, he began to suffer from attacks of "rheumatic pains" in the legs. In November, 1913, his memory failed; he became childish in his ways and behaved "like a simpleton." His aptitude for business failed, but he continued at work until January 4, 1914.

On January 14, 1914, he took to his bed. From the 16th until the 19th he lay "unconscious and delirious" with loss of movement in the right

arm, but the leg was never affected. He stayed in bed until the middle of February, 1914. When he got up he could walk well but was weak-minded and feeble and had no initiative.

On March 3, 1914, he was admitted to the London Hospital under the care of Dr. Otto Grünbaum. In the heart, lungs, abdomen and urine no abnormal signs were discovered. The temperature was raised and irregular; it varied from 99° F. (37.3° C.) to 101° F. (38.4° C.); it was usually highest in the evening. There was no tachycardia or increase in the rate of respiration.

He was childish in manner and never spoke unless addressed. He took no interest in his surroundings. He carried out movements on command in a slow irresponsible fashion after a prolonged pause for consideration. Memory was extremely defective. He could not remember any of the details of his illness, nor of the processes employed at the works where he had been foreman. He could not tell the day on which people usually go to church, nor did he know the name of the Prime Minister, though formerly he was a strong party politician. His answers to questions were frequently totally irrelevant, and he had no idea of the relationship between cause and effect. Hallucinations and delusions were not present. There was no grandeur in his ideation; he seemed to be a pure example of severe dementia and for the greater part of the twenty-four hours lay curled up in bed stuporose or asleep.

His speech was slow, phonation monotonous, and articulation defective.

He had suffered from no seizures, but for three days when in bed in January, 1914, he lay in a semi-conscious state and whilst in that condition developed a paresis of the right arm. During the whole of the year 1913 he had complained of attacks of severe headache, but on admission he made no complaint of his head and pressure of the scalp did not obviously cause pain. There was no vomiting during his stay in hospital.

Vision, as far as it could be tested, seemed to be unaffected and the optic discs and vessels appeared healthy. When roused he seemed to hear normally; smell and taste could not be tested.

The ocular muscles were unaffected, but the balance was bad and the patient could not be made to concentrate his gaze on any object for more than a few seconds. The pupils were equal in size, well centred, and reacted normally to light and accommodation. His face was much flattened and quite expressionless. The tongue was intensely unsteady on protrusion. Movements of the jaws, palate and larynx were unaffected.

The patient could hardly stand and his gait was clumsy and unsteady; this unsteadiness was not increased by closing the eyes. The balance of the fingers was bad, and fine movements of the hands could not be performed.

He complained of no spontaneous pains; no gross interference with sensibility was discovered, but the mental state of the patient did not allow of accurate testing.

The skin was oily and inactive; no local vasomotor changes were present.

The knee-jerks and ankle-jerks were brisk but ankle-clonus could not be

obtained. On the left side the plantar reflex gave a flexor response; on the right side either a sluggish extension appeared, or no response was obtained. The abdominal reflexes and the wrist- and elbow-jerks were unaffected.

Unless he were made to pass water at regular intervals he wetted the bed; apparently this was due to his mental state and not to any affection of the sphincter.

The movements of the spine were unaffected.

In the left groin and on the penis were old scars, and the tongue showed the characteristic changes of leucoplakia.

On March 11, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.2.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 256 per cubic millimetre; the pleocytosis consisted mainly of lymphocytes.

He was injected intravenously with doses of 0.9 grm. of neosalvarsan on March 12, on March 15, and on March 18, 1914. On March 31, 1914, he was discharged from hospital. Under treatment the pyrexia disappeared; he no longer wetted the bed, but his mental condition improved to a small extent only.

Here a pure dementia appeared somewhat rapidly in a man of considerable intelligence twenty years after infection. He might have been mistaken for a case of dementia paralytica without delusions if he had found his way into a workhouse infirmary; but the condition of the cerebrospinal fluid with its enormous excess of cells and negative Wassermann reaction, and also the improvement under injections of neosalvarsan, show that he was a case of the cerebral form of syphilis meningo-vascularis.

This case also illustrates the effect of the secondary cerebral destruction which so often results during the acute stage; arterial blocking and interference with the blood-supply cause secondary necrotic changes which cannot be repaired, and consequently, although the patient's condition improves rapidly, he usually shows some permanent cerebral defect. This man, unlike No 53, was a steady hard-working foreman in chemical works; he was left with a simple residual dementia and not with those defects of will and moral determination so obvious in No. 53 and young men of his group.

Sometimes, however, recovery may be so complete that the patient returns to work and appears to have regained his normal mental and physical health. Thus No. 86 was thought at first to be a case of dementia paralytica in consequence of his mental state, the seizures, affection of speech, and defective reaction of the pupils; this view was rendered more probable by the strength of the positive reaction in the cerebrospinal fluid. The short time, six years, which had elapsed

since infection alone rendered this diagnosis doubtful. However, he improved so greatly under treatment, first with iodides and then with neosalvarsan, that he has returned to full work; at the same time the Wassermann reaction has become negative in the cerebrospinal fluid, and its cell content has sunk from 63 to 2 per cubic millimetre.

A Case of Cerebral Syphilis simulating Dementia Paralytica. A strongly positive Wassermann Reaction in the Cerebrospinal Fluid became Negative under Treatment. The patient recovered completely.

Case 86.—F. J., married, valet; born 1877.

In 1906, at the age of 29, this patient contracted syphilis; he developed a sore on the penis which was followed by a rash and sore throat lasting over many months and was accompanied by chronic ill-health. He took mercurial pills for two years, between 1906 and 1908.

In 1908 he married. His wife, who is a psychasthenic subject, gives a negative Wassermann reaction in the serum; she has never been pregnant.

Soon after marriage he began to fail mentally, became irritable and forgetful and complained of attacks of severe nocturnal headache. In consequence of this failure he lost his employment and took up work as an insurance agent.

One day, towards the end of June, 1911, five years after infection, whilst riding a bicycle he had a seizure and fell off the machine. He lay on the road for some time but recovered and rode home. In September, 1911, his mental condition became so bad that he could no longer be trusted with money; he became irritable, sleepy and extremely worried. In February, 1912, he was seen by us as an out-patient; whilst attending this department he had another seizure and was in bed for three days. On March 10, 1912, he was admitted to the London Hospital.

On admission he was helpful and obedient in the wards, but was irritable, suspicious, and thought that everyone was talking about him. His attention was fleeting, his remarks inconsequent and he was with difficulty kept to the point. In the ward he rarely talked but spent much time in writing letters to sisters and doctors. These were filled with mistakes in spelling, and he missed out words and syllables; the writing itself was careless, unsteady and tremulous. His memory was extremely defective. Speech was slurred, articulation defective, and syllables were elided.

In June, 1911, he had a seizure, followed in February, 1912, by another severe one; between these dates several minor attacks occurred. He complained of intense headache and a "sense of giddiness all over the head," accompanied by pressure tenderness of the scalp. As an in-patient he vomited several times, usually in the mornings.

Vision was unaffected and the optic discs and fundi appeared natural. Smell and taste were unaffected. Hearing was fair on both sides, otorrhœa from the left ear was observed, and otoscopic examination revealed an old perforation of the drum on this side.

All ocular movements were well carried out. The pupils were equal, centred and reacted sluggishly to light and briskly to accommodation. The face was expressionless. Tremor of the lips was noticeable especially in talking, and the tongue on protrusion showed coarse irregular movements. The palate and larynx were unaffected.

The knee-jerks were exaggerated; the ankle-, elbow- and wrist-jerks were all obtained; the plantar reflexes gave flexor responses. The jaw-jerk was exaggerated.

The sphincters were controlled and the movements of the spine were well carried out.

No gross abnormalities were detected in the heart, lungs, abdomen or urine.

On March 13, 1912, the Wassermann reaction was

serum	4.4.3.3.0.
	cs.f. 4.4.4.4.0.

 and the cells numbered 63 per cubic millimetre.

The case at this time was diagnosed as one of "dementia paralytica," and he was not injected with salvarsan.

As an in-patient he improved slightly. Shortly after his discharge in April, 1912, however, he became unmanageable and was signed up and sent to an Asylum. He remained at the Asylum until February, 1913. As an in-patient there he was treated with iodides, but no mercury; gradually he improved and was discharged as "cured."

On April 12, 1913, he was readmitted to the London Hospital. At this time he was slow in action and in thought. Attention had improved and his memory was better than it had been in 1912, but was still uncertain. He slept heavily and complained of "dreams and nightmares" every night. His writing had improved greatly, was fairly steady and showed no elision of words. Speech was still slow and jerky with some slurring of syllables. Since his discharge from the Asylum he had had no seizures. He still complained of universal headache accompanied by pressure tenderness of the scalp, and was subject to frequent attacks of morning vomiting.

The right fundus oculi appeared healthy; the left, however, showed some swelling of the disc and engorgement of the vessels. Vision was good and the visual fields of normal dimensions. Hearing was fair and there was no otorrhœa.

Ocular movements were well carried out. The right pupil was larger than the left; both were regular in outline and both reacted well to light and to accommodation. The face was not so expressionless as on his previous admission in 1912. There was intense tremulousness of the lips and the tongue was jerky and unsteady in movement.

In carrying out fine movements he was still unsteady and clumsy.

He complained of spontaneous pains shooting along the arms, around the abdomen from the back and in the backs of both thighs and both calves. Areas of tenderness with over-reaction to the dragged point of a pin and other painful stimuli, and considerable sensory impairment, were present over the distribution of the second and the twelfth thoracic, and the third sacral

nerve-roots on both sides. Nowhere was any complete sensory loss found to any form of testing.

The knee-jerks were brisk and equal; the ankle-jerks, wrist-jerks and elbow-jerks were all readily obtained; the plantar responses were flexor. The abdominal reflexes were exaggerated and the jaw-jerk was brisk.

He complained of difficulty in holding his water with precipitancy of micturition, but no true incontinence.

On April 16, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.0.0.0.}$ and the cells numbered 19 per cubic millimetre.

On April 17, April 22, and April 26, 1913, he was injected with 0.9 grm. of neosalvarsan. Under this treatment the spontaneous pains disappeared, his memory improved rapidly, he gained weight and by October 20, 1913, the Wassermann reaction had become $\frac{\text{serum } 4.4.4.4.1.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells had fallen to 2 per cubic millimetre.

On November 1, 1913, he was sufficiently recovered to take up his old employment as valet and confidential servant.

§ 2.—*Hemiplegia.*

Of all the conditions due to meningo-vascular syphilis, hemiplegia is perhaps the best known and the most universally recognized. Many clinicians, however, are satisfied when they have investigated the loss of power in the limbs, tongue and face, and have determined the nature of any disturbance of speech or loss of function of the cranial nerves, which may accompany the hemiplegia.

But as soon as we become interested in the relation of these conditions to the character of the Wassermann reaction, such cases of hemiplegia obviously demand more careful examination. If any order is to be brought into the apparently chaotic results obtained from patients suffering mainly with vascular affections of the brain, we must be certain that there are no signs of disease of the spinal cord or its membranes. We shall, therefore, give two instances of hemiplegia due to meningo-vascular syphilis of the brain, in one of which the clinical signs pointed to diffuse lesions (No. 226), whilst in the other (No. 240) the disease was apparently confined to the cerebrum.

A Case of Left Hemiplegia with signs of Bilateral Affection of the Pyramidal Tracts and Local Wasting in the left Forearm and Hand. A Positive Wassermann Reaction in the Cerebrospinal Fluid.

Case 226.—G. J., male, married, dockyard policeman; born 1878. He joined the Marines as a youth and served in the Dockyards at Malta and elsewhere, from 1898 until March, 1913. He denied syphilis and gonorrhœa,

but admitted exposure. He married in 1908; his wife has never been pregnant.

From time to time during the whole of the year 1912, he was subject to severe headaches and attacks of shooting pains in his trunk and limbs.

On March 12, 1913, he was suddenly attacked with left hemiplegia for which he was admitted to the Royal Naval Hospital, Malta, where he remained until May 24, 1913. After this attack his speech became affected and his memory failed completely.

He first came under our observation in November, 1913. At that time he was dull, stupid and inattentive. His memory was extremely bad, his speech slow and slurred. He did not complain of headache and his scalp was not tender to pressure or percussion.

Vision, smell, taste and hearing were unaffected and the optic discs and fundi appeared natural.

When looking upwards the ocular balance was defective, but there was no definite paresis of any ocular muscle. The pupils were irregular in outline, oval in shape and unequal, the left much larger than the right; neither showed the slightest reaction to light or accommodation. The left half of the face moved less than the right, whilst movements of the jaws, palate, larynx and tongue were normal.

He walked on a wide base and both legs were stiff and clumsy in movement. Romberg's sign was not obtained. The muscles of the whole left upper extremity, and more especially the flexors of the left wrist, were ill-developed and weak, and the left grasp was feeble. The greatest circumference of the left forearm measured 3.5 cm. less than the right. The left thenar muscles and to a slighter extent the interosseous muscles of the left hand were wasted. There was no wasting of the right upper extremity or of either lower extremity.

Owing to the patient's defective mental state sensation could not be tested accurately, but there was no gross sensory loss.

The skin over the left hand, unlike that of the right, was moist and sodden.

The knee-jerks were exaggerated, but ankle-clonus could not be obtained. The abdominal reflexes were normal and the wrist and elbow-jerks were obtained. Both plantar reflexes gave an extensor response.

At times he wetted the bed, but complained of no difficulty in holding or passing his water.

No abnormal signs were discovered in the heart, lungs, abdomen or urine.

On November 19, 1913, the Wassermann reaction was

serum	4.4.4.4.1.
cs.f.	4.4.3.0.0.

 and the cells numbered 1 per cubic millimetre.

He was injected with doses of 0.9 grm. of neosalvarsan on November 20, November 27, and December 5, 1913. Before his discharge on December 10, his speech and mental powers had improved remarkably and under treatment with massage the wasting of the left upper extremity had begun to pass away.

A Case of Hemiplegia where the Disease was apparently confined to the Cerebrum. Negative Wassermann Reaction with Pleocytosis in the Cerebrospinal Fluid.

Case 240.—E. W., male, single, motor 'bus driver, born 1880. He denied all venereal infection, and there was no scar on the penis, but he admitted exposure on many occasions.

About May, 1913, this patient became subject to attacks of severe headache, pains in his limbs, accompanied by sweating and by mental failure. Early in October, 1913, the pains in his head became worse and he thought that he had caught a "bad cold"; then he developed weakness of the right arm and right leg and lost his taste and smell. On October 15, 1913, he did a complete day's work driving his 'bus for the full journeys, although his right arm and leg felt extremely weak. At the end of the day he collapsed in the garage and was taken home and put to bed. He slept heavily and on the morning of the 16th found that he was unable to move either his right arm or leg, but at that time his speech was not affected. He was brought up to the London Hospital and admitted under the care of Dr. Percy Kidd.

On admission he lay in a half conscious condition with his eyes closed, indifferent to his surroundings; he could be roused by shaking or by shouting, but deeply resented interference. At first speech was little affected, but on the third day after admission he became characteristically dysarthric; there was no dyspraxia. His memory was extremely defective and his attention feeble. He complained of no headache and the scalp was not tender to percussion or pressure. On the first three days after admission he vomited several times.

Smell and taste were abolished, but hearing was not impaired; vision was normal and the optic discs and fundi were unaffected.

All ocular movements could be carried out and there was no ptosis. The pupils were equal in size and reacted normally to light and accommodation. Both upper and lower portions of the right half of the face were paretic. The palate was drawn to the left on phonation and the tongue was protruded to the left. The movements of the larynx and jaws were unaffected.

Neither the right arm or leg could be moved voluntarily. The right upper extremity was flaccid, the right lower extremity somewhat spastic.

Over the right half of the trunk and extremities for the first ten days after admission the patient stated that all sensations felt "different"; but owing to his defective mental state more accurate testing was impossible. No areas of tenderness were discovered and there was no complete sensory loss.

The skin everywhere was oily and had a nauseous odour.

On the right side the knee-jerk was much exaggerated, on the left it was brisk. Ankle-clonus was present on the right side and the plantar reflex gave an extensor response; the left ankle-jerk was readily obtained and the plantar response flexor. On the right side the abdominal reflexes were completely abolished, on the left they were normal.

For five days he suffered from complete retention of urine and had difficulty in controlling his motions.

On October 23, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 31 per cubic millimetre.

He was injected on October 18, with 0.6 gm. of neosalvarsan and on October 23, October 30 and November 21, 1913, with doses of 0.9 gm.

On October 23, he developed thrombosis of the right popliteal and femoral veins with œdema of the leg.

On November 12, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 20 per cubic millimetre.

Before his discharge on November 30, 1913, his mental state and control over the right leg improved greatly, but the right arm remained completely paralysed. He continued to have difficulty in passing his urine at times. He was able to answer questions lucidly and correctly, but rarely volunteered a remark.

§ 3.—*Affections of the Cranial Nerves.*

Interference with the functions of the third, fourth, fifth, sixth, and seventh cranial nerves on one or both sides and in almost any combination are amongst the commonest manifestations of cerebrospinal syphilis. Innumerable *post-mortem* examinations have been reported showing that these signs are usually produced by endarteritis and meningeal inflammation, and such cases are usually characteristic examples of meningo-vascular syphilis (cf. Nonne [13], p. 192 *et seq.*).

We venture, however, to cite the following cases of this well-known condition because they illustrate the different results which may be obtained with the Wassermann reaction in the cerebrospinal fluid, when meningo-vascular syphilis attacks the cranial nerves and brain-stem. Nowhere are the results of this reaction at first sight more confusing and we shall attempt to show how, in most cases, the explanation of these differences can only be discovered by careful study of the clinical manifestations.

Our first instance (No. 74) is a man, aged 38, who began to suffer from cerebral symptoms seven years after infection. These continued with intermissions for ten years; he then developed an unsteadiness in movements of the eyes, weakness of the right half of the face and palate, together with a bilateral affection of the pyramidal tracts. The Wassermann reaction in the cerebrospinal fluid was at first strongly positive, but became negative in nine months under treatment with neosalvarsan.

The second case (No. 253) was an elderly man, infected twelve years before, who showed all the signs of a complete third nerve paralysis,

associated with pain and loss of sensation over the superior division of the trigeminal nerve. Unfortunately he did not come under our care until he had already received three injections of 0.9 grm. of neo-salvarsan; but in spite of the great improvement in symptoms which followed this treatment he still showed a positive reaction in the cerebrospinal fluid at our first examination, eight months later.

Our next instance (No. 310) is a case of affection of the left crus cerebri, fourteen months after infection, showing the usual signs of paralysis of the third cranial nerve associated with a crossed hemiplegia. The Wassermann reaction was negative in the serum, but weakly positive in the cerebrospinal fluid.

In the next case (No. 128) the signs of complete paralysis of the third nerve were not accompanied by any other evidence of intracranial disease. Here the reaction of the cerebrospinal fluid was at first weakly positive, but became negative within eight weeks of the first injection. The meningo-vascular lesions, revealed by the clinical signs and symptoms, were less widespread than in the previous cases, and consequently the Wassermann reaction was weakly positive in the cerebrospinal fluid.

This leads us on to cases like No. 92, where from the first the Wassermann reaction was negative in the cerebrospinal fluid. This man suffered from paralysis of the left half of the palate, left vocal cord and left sterno-mastoid, which came on suddenly within eighteen months of infection.

One of the most remarkable consequences of syphilitic affection of the brain-stem is polyuria associated with polydipsia; we give an example of this condition (No. 149), where the reaction of the pupils became affected under observation. Here the Wassermann reaction was also negative in the cerebrospinal fluid (cf. Oppenheim [16], p. 53).

Thus in uncomplicated cases of disease of the cranial nerves the behaviour of the Wassermann reaction in the cerebrospinal fluid depends largely on the extent of the intracranial lesions revealed by the signs and symptoms.

But in order that this rule may be true in practice, it is most important to exclude all cases where there is clinical evidence of some concomitant affection of the spinal meninges and roots. This complication of cranial nerve paralysis is commoner than is usually supposed, and failure to appreciate this intraspinal affection will make it impossible to understand the behaviour of the Wassermann reaction in these cases. For a slight disturbance of some cranial nerve may be asso-

ciated with an intensely positive reaction in the cerebrospinal fluid if meningo-vascular changes are also present within the spinal canal.

We have, therefore, added two instances (No. 189 and No. 262) where comparatively trivial affections of the cranial nerves were accompanied by a strongly positive reaction in the cerebrospinal fluid, due to the simultaneous affection of thoracic nerve-roots. Had it not been for careful clinical tests, the true explanation of this reaction in the cerebrospinal fluid would have been missed, and our statistical conclusions would have become chaotic.

A Case of Affection of several Cranial Nerves on both sides. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which became Negative within Nine Months under Treatment.

Case 74.—S. H., male, married, book packer; born 1873. In September, 1895, at the age of 22 he contracted syphilis and developed a chancre, followed by a bubo in the right groin. He was treated for three months and suffered from no secondary manifestations. On his discharge from the Army, in 1902, he married; by him his wife has had (1) a miscarriage in 1903; (2) a miscarriage in 1903; (3) a girl born in 1904; (4) a girl born in 1906, both of whom survived, and are healthy.

In 1902, shortly after marriage, he became subject to attacks of headache, vomiting, and giddiness, called by the patient "bilious attacks." Later, in the same year, he had a seizure accompanied by much headache, some vomiting, and followed by unsteadiness in walking, with numbness of the right leg. After this seizure he attended at the National Hospital, Queen Square, as an out-patient for two years, and was treated with mercury and iodides. He gradually improved, and was in fair health, between 1903 and 1905, except for "bilious attacks."

In 1905 he had another "bad turn," with recurrence of the headache, vomiting, and giddiness, together with a feeling of falling to the right and numbness of the right leg; this attack lasted for about three months.

During the years 1905 to 1912, except for attacks of headache, usually in the frontal region, his health was good, and he was rarely away from business.

In November, 1912, seven weeks before admission to the London Hospital, he went to bed one night feeling fairly well; on the following morning he woke with an intense headache, accompanied by giddiness, retching, and vomiting. On the next day, when he tried to walk, he found that he was unsteady on his legs, and "everything seemed to be going round." After this attack he began to complain of shooting pains and numbness in both legs. He found that either he could not pass urine on desire, or that he was unable to wait long enough to prevent wetting himself.

On admission to Hospital on January 4, 1913, he was found to have thickened and tortuous vessels; the right radial pulse was fuller than the left. The heart was not enlarged, and the cardiac sounds were clear. No

abnormal signs were discovered in the lungs, abdomen, and urine. The temperature was not raised.

His mental state was normal, but he complained of bilateral headache chiefly in the frontal region, and the scalp was tender to pressure and percussion. He had had several attacks of vomiting, the last of which occurred on November 28, 1912.

The fundi appeared healthy, and hearing, smell, and taste were unaffected.

There was a general unsteadiness in ocular movements, which was best observed when the patient turned his eyes laterally; but he complained of no diplopia. The pupils were equal and of moderate size; they reacted well to light and on accommodation. There was no sensory or motor affection of the trigeminal. There was some weakness of the right facial muscles, especially when he attempted to close the right eye. The palate was drawn to the left on phonation, but the vocal cords moved naturally, and there was no difficulty in swallowing. The muscles supplied by the spinal accessory nerve were unaffected. The tongue deviated to the left on protrusion.

He walked uncertainly on a broad base, using his right leg as a prop, and when the eyes were closed fell towards the right. The grasps were powerful, and co-ordination of the hands was carried out fairly well. Dysdiadokokinesia was absent.

He complained of few spontaneous pains, and no loss of sensibility could be discovered.

The knee-jerks on both sides were clonic, the ankle-jerks were extremely brisk, but there was no ankle-clonus. Wrist- and elbow-jerks were readily obtained, and the jaw-jerk was present. The plantar responses on both sides were extensor. The upper and lower abdominal reflexes and the cremasteric reflexes could not be obtained.

The patient complained that he could not hold his urine, nor start the act of micturition at will, but he could control the motions of his bowels.

On January 8, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 4.4.4.3.1.}$

On January 14, 1913, he was injected with 0.9 gm. of neosalvarsan, and this dose was repeated on January 22, and again on January 29, 1913. After treatment his general condition improved rapidly, the headache ceased, and he gained weight.

He was again admitted for investigation and treatment on September 25, 1913. He then stated that since the first set of injections he had ceased to suffer from headaches and attacks of vomiting. The ocular movements were still unsteady. The right half of the face was weak. The movements of the palate were now normal, but the tongue still deviated to the left on protrusion. He walked uncertainly on a broad base, and the right leg was stiff and clumsy. The reflexes were exactly as before, and he still had difficulty in holding water and in starting the act of micturition.

On September 24, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f. } 0.0.0.0.0.}$

*A Case of Third Nerve Paralysis with some Affection of other Cranial Nerves.
A Positive Wassermann Reaction in the Cerebrospinal Fluid.*

Case 253.—T. G. F., male, married, compositor; born 1857. In 1901, at the age of 44, this patient contracted syphilis; he suffered from a sore on the penis which was diagnosed as syphilitic, but was treated by a chemist for two months only. No manifestations of secondary syphilis followed.

About the beginning of the year 1913 he began to suffer from attacks of severe headache, feelings of tiredness and failing memory. On June 23, 1913, the headache suddenly became worse, a "sort of neuralgia just above the right eye" with "jumping and darting pains." On the morning of June 25 he woke to find that he "saw double." On the 27th he found that the right eyelid had dropped, but "when the lid was opened he saw things as before." From the 23rd to the 30th he was extremely irritable and restless; he said that he had not slept for five nights before his admission on July 1 because of the "horrible pains in the head." On June 30 he completely lost the power of moving the right upper eyelid.

On admission on July 1, 1913, he was mentally clear, but answered questions slowly and with difficulty. His memory was defective for the events of the preceding weeks, but distant memory was unimpaired. He complained that he "kept on seeing strange sights whenever he closed his eyes," and that at home, whilst he was in bed, "the bells seemed to be ringing." At night he was restless and complained of nightmare.

For his work as a compositor he had relied upon his right eye, which he said was "the master"; but to tests he now saw more plainly and distinctly with the left. Both visual fields were of normal extent.

On ophthalmoscopic examination both optic discs and fundi appeared healthy. He was slightly deaf but there was no evidence of internal ear deafness. Smell and taste were unimpaired.

He had suffered neither from seizures nor attacks of vomiting.

He was unable to raise the right upper eyelid. He could move the right eyeball to a small extent outwards and upwards. The muscles supplied by the right third cranial nerve were totally paralysed. The right pupil was ovoid in shape, irregular in outline and larger than the left; it neither reacted to the strongest lights nor to accommodation. Movements of the left eyeball were unaffected. The left pupil was small and reacted naturally to light and accommodation.

He suffered from headache passing from the forehead to the nape of the neck mainly on the right half of the head, which was uniformly tender to pressure. He also complained of pains over the right half of the forehead. Here there was a considerable area of tenderness within which the skin reacted excessively to the point of a pin lightly dragged across it; at the same time the sensation seemed "altered and dulled." Elsewhere over the distribution of the trigeminal, sensibility was unaffected.

On opening the mouth widely the jaw swung over to the right, and on the right side the masseter contracted feebly. The face was expressionless, but

all movements were possible; at rest the right half tended to overact. The movements of the palate and larynx were unaffected. The tongue was protruded straight, but could not be held steadily.

The gait was normal and no change could be detected in motion, sensation, the reflexes, or the action of the sphincters.

On July 8, July 11, and July 18, he was given doses of 0.9 grm. of neosalvarsan. On his discharge on July 22, 1913, although the signs were unchanged he no longer complained of headache or of pain in the right orbital region.

On March 2, 1914, he was readmitted to Hospital. At this time the movements of the right eyeball were considerably more extensive than they had been in the previous July. The lateral movements were well performed but all upward and downward movements were completely lost. The drooping of the right eyelid was less extreme. The right pupil was completely fixed both to light and to accommodation, whilst the left pupil reacted normally. The neuralgic pain and interference with the sensibility of the skin over the right half of the forehead had entirely disappeared, but on the left side a similar tender area was present over the front of the hairy scalp. The skin over this area responded excessively to the dragged point of a pin and to pinching, but was not tender to pressure and over it no loss of sensibility was discovered. The movements of the jaw were well performed and the facial movements were natural. There was no difficulty with swallowing, and the movements of the palate and larynx were unaffected. On protrusion, the tongue deviated to the right and could not be held steadily.

Taste, smell and vision were unaffected. He was slightly deaf, probably owing to wax, as there was no evidence of any affection of the internal ear or nerve-deafness.

Apart from these signs of interference with the cranial nerves no signs were discovered of any gross disease elsewhere in the nervous system.

On March 4, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.0.0.0.}$ and the cells in the cerebrospinal fluid numbered less than 1 per cubic millimetre.

A Case of Affection of the Left Crus Cerebri; Right Hemiplegia, with Paralysis of Parts supplied by the left Third Cranial Nerve. Negative Wassermann Reaction in the Serum, Positive Reaction in the Cerebrospinal Fluid.

Case 310.—G. W., male, married, aged 36, butcher; born in 1878. In January, 1913, this patient contracted syphilis. He developed a hard chancre, followed by general malaise, ulceration of the throat which lasted for three or four months, and a generalized syphilitic rash. He was treated with mercury by the mouth for nine months.

About November, 1913, his mental condition failed and he became subject to severe attacks of headache. On December 24, 1913, he was seized with pains in the back and an extremely severe headache, which in the course

of the day was followed by tremor and some difficulty in moving the right arm and leg; before evening the right arm shook so badly that he could not hold small objects in his hand. He was treated for "neurasthenia" and gradually improved. On February 14, 1914, he went for a holiday to the seaside and whilst away, on February 27, the left eyelid dropped and the right side of the face became paralysed. He was put to bed and shortly afterwards developed the stuporose condition in which he was admitted to the London Hospital on March 14, 1914, under the care of Dr. Theodore Thompson.

The patient was a well-developed, muscular man. His skin was oily and had a nauseous odour. His temperature before treatment oscillated between 97.5° F. (36.4° C.) and 99.8° F. (37.7° C.) The rate of the pulse was not increased, but the cardiac sounds were muffled and indistinct. No abnormal signs were discovered in the lungs or abdomen and the urine contained neither albumen nor sugar.

He was somnolent and stuporose, but could be roused by shouting and then answered questions in an illogical, inconsequent manner. Frequently he repeated words and sentences several times before he attempted to respond, and then gave an answer which was irrelevant or made a movement which had little or no relation to the command given. He rarely spoke spontaneously. He lay in bed sleepily with his eyes closed for the greater portion of the twenty-four hours, but at times he roused himself and became restless and difficult to manage. His voice was monotonous and many syllables and words were slurred. He yawned frequently. Delusions and hallucinations were not present. He complained of no headache and seemed happy and contented. He did not suffer from fits or attacks of vomiting.

He complained of diplopia and mistiness of vision; on ophthalmoscopic examination the optic discs and fundi on both sides appeared healthy. He responded extremely slowly to all auditory stimuli, but there was no deafness due to disease either of the internal or middle ear. Smell and taste were unaffected.

The movements of the right eyelids and eyeball were natural. The right pupil was well centred, of average size and reacted normally to light and on convergence. The left upper lid was dropped. The movements upwards and inwards of the left eyeball were extremely defective. The left pupil was dilated; it neither reacted to strong lights nor on attempts at convergence. The movements of the palate, larynx and jaws were unaffected. The tongue could not be held steadily and on protrusion it deviated to the left. He complained of difficulty in swallowing and often had to be fed with a nasal tube. The movements of the sterno-mastoids and trapezii were normal.

He could not stand and all movements of the arms and legs were clumsily performed and paretic. The right grip was feeble, the left fairly strong. The alignment of the fingers and wrist on the right side was bad and they could not be held steadily. The power of both legs was much impaired, the right to a greater degree than the left. At times he was restless and waved his limbs about in an inco-ordinate manner.

He complained of no spontaneous pains and no sensory loss could be discovered. The vibrations of the tuning-fork and the shape, size, and form of objects placed in the hands were well recognized.

The right knee-jerk was greatly exaggerated, the left was present. Ankle-clonus was readily elicited on the right side, but could not be obtained on the left. On the right side the plantar reflex gave an extensor, on the left a flexor response. The wrist- and elbow-jerks on the right side were exaggerated. The right abdominal reflexes were almost completely abolished.

On admission he passed urine and faeces incontinently into the bed.

On March 18, 1914, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 4.1.0.0.0.}$ and the cells numbered 39 per cubic millimetre.

He was injected with 0.3 gm. of neosalvarsan on March 18, 0.6 gm. on March 20, and 0.9 gm. on March 23, March 25 and March 27, 1914; he also received intramuscular injections of 0.002 gm. of hydrargyri perchloridi three times daily between March 20 and April 9, and 2 gm. of potassium iodide three times daily by the mouth.

Under this treatment the signs of a lesion within the brain-stem persisted unchanged, but the mental condition brightened and he became more rational and less drowsy.

The Wassermann reaction on May 13, 1914, was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 13 per cubic millimetre.

Paralysis of the Third Cranial Nerve with a Positive Wassermann Reaction in the Cerebrospinal Fluid, which became Negative within eight weeks.

Case 128.—F. R., male, married, labourer; born 1866. In 1884, at the age of 18, this patient contracted a "running." He had no recollection of any sore, or any manifestation of secondary syphilis. He married for the first time in 1885; of this marriage there were no children, and this wife died of chronic pulmonary tuberculosis at the age of 28. He married his second wife in 1893; by her he had two children, the one born in 1894 and the second born in 1903.

Until the beginning of the year 1913 his health was fairly good, but on February 15, 1913, he noticed that his left eyelid had dropped. During the next seven days complete paralysis of the left third cranial nerve developed which began with troublesome double vision lasting two days.

On admission on February 22, 1913, there was complete paralysis of the left third cranial nerve with ptosis, diplopia on looking upwards and downwards, and a large fixed pupil. The external rectus and superior oblique muscles on this side acted perfectly and the movements of the right eyeball and pupil were unaffected. Vision and visual fields on both sides were normal and both fundi and discs appeared healthy. No further physical signs of nervous or other disease were discovered. A scar was seen on the penis and the shins showed typical tissue-paper scars.

On March 5, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.1.0.0.0.}$ and the cells numbered 11 per cubic millimetre.

He was injected with 0.9 gm. of neosalvarsan on February 25, 1913, and this dose was repeated on March 8.

On April 23, 1913, the physical signs were unchanged, but the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 11 per cubic millimetre.

In May, 1914, he still showed an almost complete paralysis of the left third cranial nerve, but in the twelve months since he was first treated no new manifestations had appeared.

A Case of Paralysis of the Palate, the Vocal Cord, the Trapezius and Sternomastoid on the left side. Root Lesions of the Left Upper Cervical Nerves. Medullary "Fits" and Glycosuria following Injections of Neosalvarsan.

Case 92.—H. K., male, single, hairdresser; born 1892. In the autumn of 1911, at the age of 19, the patient caught syphilis. He developed a chancre, but no rash or other secondary manifestations followed. He attended twice at the Lock Hospital; at the end of this time the chancre had completely healed.

His health then remained fairly good until October, 1912, when he began to complain of left-sided headache "in the temples" and earache on the left side. He attended the London Hospital for some weeks under the care of Dr. Lambert Lack.

On January 13, 1913, after a period during which he complained of "buzzings in the left ear," he suddenly lost his voice and became unable to swallow. "My throat became as if it should have been sore but was not." Then he became subject to pains shooting down the left side of the neck to the point of the left shoulder, and became "depressed."

On February 25, 1913, he was admitted to the London Hospital. On admission he complained of severe pains in the left side of the neck, difficulty in swallowing, an alteration in his voice, intense thirst, mental depression, and left-sided temporo-occipital headache with severe pain over the left external auditory meatus.

He was very emotional, but attention and memory were good and he slept well.

Ocular movements were well carried out and he had never complained of double vision. The pupils were well centred and reacted naturally to light and accommodation. The face acted normally on emotion and on voluntary movement. Movements of the jaws were well performed, and there was no alteration in the sensibility of the skin supplied by the fifth cranial nerve.

On phonation the palate was drawn up to the right, owing to complete paralysis of the left half. At times he had difficulty in swallowing solids; he never experienced any difficulty in swallowing fluids, and the difficulty with solids varied much from time to time. He showed no tachycardia and no

alteration in the respiratory rhythm. The left vocal cord lay in the "cadaveric" position and was immobile on phonation. The left shoulder was dropped and the sternomastoid and trapezius muscles on this side were paretic and wasted, more especially their upper halves. The levator anguli scapulæ and other muscles of the shoulder region were unaffected. The tongue showed no wasting or fibrillary twitchings, and was protruded straight.

Vision and the optic discs on both sides were unaffected.

He complained of noises and "buzzings" in the left ear, but no definite loss of hearing could be determined on examination. Smell and taste were unaffected.

The limbs were fairly well developed and no local wasting of muscles was present. The hands were steady and the fingers well aligned. The grips and gait were natural.

He complained of pains in the left side of the neck and over the distribution of the second, third and fourth cervical roots, on the left side tenderness was present to the dragged point of a pin and to pinching the skin. The back of the pharynx and the fauces were totally insensitive to a brush.

All the reflexes were normal. The knee-jerks were readily obtained and both plantar reflexes gave a flexor response. The sphincters were unaffected.

The heart, lungs and abdomen showed no abnormal physical signs, and on admission the urine contained neither albumen nor sugar. A scar was visible on the penis and another was seen due to old and recent inflammation on the front of the right shin. The bone under the scar on the right shin was thickened (gummatous periostitis).

On March 7, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 0.0.0.0.0.}$

On March 7, March 12, and again on March 18, 1913, he was injected intravenously with 0.9 grm. of neosalvarsan.

On March 16, 1913, the patient had seven "medullary fits," in which he became cyanosed, developed bradycardia, became drowsy and the temperature rose to 100° F. (37.8° C.). After these attacks glucose and aceto-acetic acid appeared in the urine. On March 17, 1913, the urine contained 0.7 per cent. glucose and gave a definite Gerhard and Rothera reaction for aceto-acetic acid. The glycosuria persisted for forty-eight hours after the onset of these attacks.

On April 15, 1913, the physical signs remained unchanged, except that the movements of the palate were now symmetrical and there was no glycosuria. The patient no longer complained either of headache or of noises in the ears.

A Case of Polydipsia with Polyuria and Recurrent Attacks of Pyrexia due to Syphilis. Subsequent Development of Defective Pupillary Reactions.

Case 149.—B. S., male, single, labourer; born 1885. In 1906, at the age of 21, he contracted a chancre, for which he was treated for six weeks; no secondary manifestations followed, and he remained in perfect health.

In July, 1912, six weeks before his first admission to the London Hospital,

under the care of Dr. Percy Kidd, he began to suffer from a severe dull headache, which was worse towards evening and when he was lying down. Two weeks afterwards he took to his bed with a febrile illness diagnosed as "typhoid fever"; the fever lasted until admission to hospital four weeks later and was accompanied by intense thirst and polyuria.

On admission, on August 20, 1912, he was a well-covered healthy man, complaining of severe headache and great thirst. He was somnolent, introspective and inattentive. His scalp was everywhere exquisitely tender to pressure. The cranial nerves, motion, sensation, the reflexes and the special senses were unaffected.

His temperature was 102° F. (39° C.), the rate of the pulse 120 per minute, and the rate of respirations 24 per minute. The quantity of urine passed in twenty-four hours varied from 5,700 to 9,000 c.c., but albumen and sugar were not present.

On August 28, 1912, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.2.}}{\text{cs.f. 0.0.0.0.0.}}$

On August 24, after three days strict confinement to bed, the temperature fell to normal.

On August 30, 1912, he received 0.9 gm. of neosalvarsan intravenously and similar doses on September 3 and 9. Under treatment the headache had disappeared, but the polydipsia and polyuria persisted for some weeks unchanged.

On October 12, 1912, his headache reappeared in a different form. After some trouble at home he had a seizure in which he "seemed to come over giddy"; his head was "bad behind the eyes" and he again became irritable and introspective, complaining of pains all over the body.

On November 11, 1912, he was readmitted; at that time he was dull and somnolent and altered mentally. The right pupil was now widely dilated, whilst the left was of normal size; both reacted sluggishly to light and immediately dilated again; the reaction to accommodation was normal. The tongue could not be held steadily. Otherwise no abnormal signs were discovered in the nervous system. The quantity of urine passed on this occasion was still high and on an average 3,000 c.c. in twenty-four hours. On

November 12, 1912, the Wassermann reaction was $\frac{\text{serum 4.3.2.1.0.}}{\text{cs.f. 0.0.0.0.0.}}$

He was readmitted on January 4, 1913, complaining of "general pains and muzziness of the head," but there was no polyuria and the daily quantity of urine passed was, on an average, 1,200 c.c. On February 5, 1913, the

Wassermann reaction was $\frac{\text{serum 3.3.3.2.1.}}{\text{cs.f. 0.0.0.0.0.}}$

Since this time he has been continuously under observation and has had three distinct pyrexial attacks followed by intense polyuria similar to that observed when he was first admitted in August, 1912.

On November 4, 1912, January 22, 1913, and on September 23, 1913, he was given injections of 0.9 gm. of neosalvarsan.

On September 24, 1913, the Wassermann reaction was $\frac{\text{serum 2.0.0.0.0.}}{\text{cs.f. 0.0.0.0.0.}}$

Affection of many Cranial Nerves, together with several Spinal Roots. Positive Wassermann Reaction in the Cerebrospinal Fluid.

Case 189.—A. O., male, married, electrician; born 1858. This patient joined the Army in 1875, transferred himself to the Marines in 1877, and then travelled round the world "having a good time" from 1885 to 1886.

He denied syphilitic infection, but admitted frequent exposure, and in 1883 he suffered from an illness called "malaria," with a rash, fever, and aching all over. He married in 1886 and his wife had five children born between 1887 and 1894, all of whom survive and are healthy.

In March, 1912, he began to suffer from "sciatica," shooting pains in the back and inner side of the right thigh. These pains were severe for four or five months, and towards the end of the attack were accompanied by a feeling of tightness and shooting pains in the lower abdomen. He was admitted to the General Hospital, Detroit, in June, 1912, and remained there until December, 1912. Under treatment with rest and morphia the pains became easier.

In October, 1912, a lump appeared at the angle of the right lower jaw; this was excised on March 6, 1913, and proved on microscopical examination to consist of gummatous material. Towards the end of March, 1913, the right half of his face and the right eye became "dead and numb." Then the right eye seemed to become "stiff and dry" and ceased to secrete tears, and he completely lost smell and taste. He wasted rapidly, and between January, 1912, and June, 1913, his weight fell from 11st. 2 lb. to 8 st. 9 lb. (from 71 to 55 kilos).

On April 5, 1913, he left the United States feeling "tired and good for nothing." On the voyage home he developed a squint and later diplopia; at the same time he began to suffer from severe pains in the head and found difficulty in moving his jaws and tongue.

He was seen by one of us on June 17, 1913, and admitted to the London Hospital under the care of Dr. Percy Kidd. On admission he was a wasted, worn man. His memory and attention were good and speech was unaffected. He had not suffered from seizures or attacks of vomiting. He complained of headache passing from the frontal region through the temples into the back of the neck, worse on the right side than on the left, and the scalp over these regions was tender to pressure.

Smell was completely abolished and taste was almost lost. He said that objects appeared hazy and misty, but though the vessels of the fundi were engorged and pinker than normal, the optic discs appeared healthy. On both sides hearing was impaired and he could hear a watch at the distance of 3 cm. only, which could be heard well by a normal person at 40 cm. On the right side bone-conduction was more defective than on the left.

He suffered from a permanent right-sided squint and complained of diplopia. The right external rectus muscle was completely paralysed, the left acted normally. The muscles supplied by the 3rd and 4th cranial nerves on both sides

acted powerfully. The pupils were well centred and reacted briskly to light and accommodation, but to light the reaction was ill-sustained and was accompanied by hippus.

He complained that his artificial teeth could no longer be made to fit; on opening his mouth widely the jaw swung over to the left and the right masseter and temporal muscles on volition contracted feebly. He complained of shooting neuralgic pains and numbness over the whole of the skin supplied by the right trigeminal nerve. Over this area there was gross sensory loss of sensibility to the prick of a pin, to the hot and cold tubes, and to the light touch of cotton-wool.

The palpebral fissures were equal and the movements of the frontalis symmetrical, but there was much weakness of the lower portion of the right half of the face.

On phonation the uvula was drawn up to the left; the tongue was protruded towards the right, although the left half was also weak; he said that the tongue felt too big for his mouth and would not "do its work."

Swallowing was unaffected and the movements of the larynx were normal.

The trapezii and sternomastoid muscles were well developed. There was no polydipsia or polyuria.

The gait was somewhat rolling and unsteady, but Romberg's sign was not present. The grasp of the left hand was feeble and in movement this hand was clumsy. A definite static tremor of the left upper extremity appeared when the hands were stretched out in front of the trunk. The patient experienced no difficulty in rapidly rotating the wrists. The lower abdominal muscles, more especially on the right side, were paretic, and the patient's abdominal wall bulged when he raised his head from the bed. The muscles on the inner side and along the back of the right thigh were somewhat wasted.

The patient complained of (i) spontaneous neuralgic pains in the right side of the face; (ii) of tightness in the right half of the abdomen and back above and below the level of the umbilicus; (iii) shooting pains in the front of the thigh and over the lower part of the abdomen on the right side; (iv) of shooting pains over the back of the right thigh and calf. The skin in these regions on the trunk and lower extremity was tender and reacted excessively to the dragged point of a pin. At the same time there was some sensory loss over those areas to the prick of a pin. The areas corresponded to the peripheral distribution of the 9th, 10th and 12th thoracic, the 1st lumbar and the 2nd and 3rd sacral nerve-roots on the right side.

The knee-jerks were exaggerated, the left brisker than the right; both ankle-jerks were readily obtained, but ankle-clonus was not present. On the right side the plantar reflex gave a flexor, on the left an extensor response. The wrist- and elbow-jerks on the left side were brisker than on the right. Abdominal reflexes could not be obtained.

Previous to his admission he had experienced difficulty in holding his water, but whilst under observation this was no longer present.

No abnormal physical signs were discovered in the heart, lungs or abdomen, and the urine contained neither albumen nor sugar.

On June 25, 1913, the Wassermann reaction was

serum	4.4.-.-.
cs.f.	4.4.4.0.0.

and the cells numbered 70 cubic millimetres.

He was injected on June 27, July 5, and July 10, 1913, with 0.9 gm. of neosalvarsan. Before his return to America in October, 1913, he had improved greatly. All spontaneous pains had ceased, he walked well and no longer complained of the difficulty with his mouth and jaws.

Affection of the Trigeminal, Auditory, Vestibular, and Glossopharyngeal Nerves, together with some Spinal Nerve-roots. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which became Negative under Treatment.

Case 262.—H. O., male, married, cabinet maker; born 1884. In 1903, at the age of 19, he contracted syphilis and suffered from a hard chancre which was not followed by any manifestations of secondary syphilis; the sore healed in a few weeks without treatment.

In 1905 he was admitted as an in-patient into the Seamen's Hospital, Greenwich, where he remained six months, complaining of pains in many joints and in the heels and back of the calves.

He married in 1907; of this marriage a healthy child was born in 1908, in whose serum the Wassermann reaction was negative; his wife had had no miscarriages.

In 1909 he suffered from a rash on the back of both forearms, lasting a few weeks only, and about the same time a gumma developed on the left shin which healed under the administration of iodides.

Between 1909 and the summer of 1912 his health was good, but in the autumn of 1912 he began to complain of pains in the head, passing from the lower part of the forehead along the temples into the back of the neck: he described the pains as "gnawing and continuous, like the rheumatics." The pains at first came on in attacks only; in 1912 he suffered from an attack about once a week, but later they became more frequent, lasted longer and "left his head sore." About June, 1913, his scalp became so tender that "he could no longer wear a hat." He said that the pains were always worse when he was in bed at night, and when he was at work; they were especially aggravated by the noise of the machinery; at times when the pains were severe he felt sick, but he had never actually vomited.

About May, 1913, he became drowsy by day, but began to sleep extremely badly. Then he became subject to "dreadful nightmares"; he would wake up in "frights" thinking that a "circular saw was cutting off his fingers and the like."

He continued at work until the middle of October, 1913. One evening in that month, whilst playing ludo with his wife, he seemed to "come over giddy" and fell off his chair. He was helped to bed, where he remained in a half-conscious condition for three days; he was away from work at this time for three weeks. Then, after working for nine days, he had a second attack of giddiness in the workshop. He felt "as if falling backwards and to

the left," sat down, became dazed but did not actually fall or lose consciousness. After this attack until the time of his admission to the Hospital he did no work. Between the middle of November, 1913, and February, 1914, he had five distinct "giddy" attacks, and on three separate occasions actually fell in the street. Between them, whenever he closed his eyes he had a feeling "as if he were falling backwards and to the left." This feeling of falling was intensified by lying on his left side. During the attacks the whole world seemed to become misty and fade away, and "things seemed to move away to the left to a buzzing noise in the left ear"; apart from the attacks he had never heard this noise in his ear. In the attacks he never actually lost consciousness, but on one occasion he voided urine. After the attacks he usually found that a tender spot had appeared below and behind the auditory meatus on the left side. Between the attacks he was drowsy and dazed, and so unsteady on his legs that he was unable to stand without support.

About October, 1913, he began to suffer from a series of shooting "rheumatic" pains in the right arm, forearm, and ulnar fingers. From that time he had also experienced a "tight, funny sensation" in his abdomen at about the level of the umbilicus, passing round the sides into the back at a slightly higher level.

He also volunteered the statement that since the illness began he had gradually lost his memory, become less able to concentrate his thoughts, was no longer able to look after money matters, and "had lost all his knack with his fingers."

He was admitted to the London Hospital, under the care of Dr. Robert Hutchison, on February 13, 1914.

On the penis was the scar of a chancre; gummatous scars were present on the left shin and a raised tender swelling, evidently a gumma of the peritoneum, was present on his right shin. A peculiar herpetiform rash occupied the skin of the nose, whilst both forearms were covered with a raised, scaly itching, circinate eruption, which had been present for eighteen months.

He was irritable, passionate and excitable. He acknowledged that he was less capable in business than he had been formerly and that as a handicraftsman he had lost all his habitual skill. His memory for recent events was defective, but fair for past events. His attention was impaired. He spelt badly and was restless at nights. His speech was natural. Under observation he suffered from no fits or attacks of giddiness, nor did he vomit. He complained of a constant, intense headache which was increased by noise or sitting in front of the fire. The whole of his scalp was exquisitely tender to pressure.

Vision, smell and taste were unaffected, but the vessels of the fundi were engorged and tortuous; there was, however, no swelling of the disc or œdema of the fundus. Hearing on the left side was impaired, and tests showed that this was due to an affection of the internal ear or auditory nerve; on the right side hearing was unaffected.

Irregular movements of the eyeballs appeared on extreme lateral movement, but there was no true nystagmus. The eyes were prominent, but there was no paresis of any ocular muscle and diplopia was absent. The pupils reacted slowly to light with the appearance of rhythmic contractions and dilatations; they were equal in size, well centred and reacted normally on convergence and accommodation. The facial movements were unaffected and the muscles of the left half showed less tone than those of the right. The movements of the jaw were natural. He complained of spontaneous pains of a "neuralgic" character in the left side of the face above the malar bone passing back to the line of the scalp and as far forward as the middle line of the forehead. Over this area the skin was tender and showed over-reaction to the dragged point of a pin together with some diminution, but no complete loss of sensibility to pin-prick, heat or cold; no change could be discovered on testing with cotton-wool. On phonation the uvula was drawn up to the right but the tongue was protruded straight and held steadily, and the movements of the larynx were unaffected. The trapezii and sternomastoids were well developed and swallowing was unaffected.

His gait was rolling and ataxic; he tended to fall to the left when his eyes were open and could not stand when his eyes were closed. When he was made to walk round a chair he fell inwards when walking counter-clockwise and outwards when walking clockwise. When he crawled the left shoulder drooped and he tended to roll over towards the left. The tone of the muscles of the left upper extremity was less than of the right. He experienced great difficulty in rapidly rotating his left hand, and this hand was clumsy in performing co-ordinated movements. There was no hypotonia of the legs and no local muscular wasting.

He complained of spontaneous pains (i) in the left side of the face; (ii) in the right axilla and along the inner border of the arm and to a less extent of the forearm, which he called the "rheumatics of the arms"; similar pains occasionally also appeared on the left side, but these were less constant and less severe; (iii) tight feelings and shooting pains in the abdomen at the level of the umbilicus, passing round to the back at a somewhat higher level; (iv) shooting pains at the back of the right and left thighs below the buttocks and in the back of the calves ("rheumatics in the legs"). To the dragged point of a pin and to pinching of the skin areas of tenderness were discovered, corresponding with the peripheral distribution of the ophthalmic division of the left trigeminal nerve, of the 2nd, 3rd, and 10th thoracic, and of the 2nd and 3rd sacral nerve-roots on both sides. The tender area supplied by the 10th thoracic nerve-roots showed a considerable loss of sensibility to the prick of a pin and to the hot and cold tubes. The vibrations of a tuning-fork and passive movement and posture were well recognized everywhere.

The knee-jerks were obtained and equal, the ankle-jerks were normal. On the left side the plantar reflex gave a flexor, on the right an extensor response. The abdominal reflexes and the wrist- and elbow-jerks were natural.

He experienced no difficulty in holding or passing water.

No abnormal physical signs were discovered in the heart, lungs, abdomen or urine.

On February 19, 1914, the Wassermann reaction was

serum	4.4.4.4.4.
cs.f.	4.4.4.4.0.

and the cells numbered 55 per cubic millimetre.

He was injected on February 18, February 21, and March 2, 1914, with doses of 0.9 gm. of neosalvarsan.

After treatment he improved slowly and gradually. The headaches ceased, his memory and aptitude returned, he began to sleep normally and was no longer troubled with dreams or restless nights. He returned to work on April 6, 1914; he was then able to carry out his work up to his old standard and earn full wages. On April 24, 1914, he had a slight attack of the "old giddy sensations." When seen on May 3, 1914, the skin rashes had disappeared and the gumma on the right shin was no longer evident. All the areas of tenderness had disappeared, and he no longer complained of the "rheumatics." He was not subject to any headaches and his scalp was no longer tender. Hearing had improved and the signs of left-sided deafness were no longer demonstrable. The fundi appeared natural and the reaction of the pupils was normal. Ataxy and Romberg's sign were not present. He walked well. The plantar reflexes now gave flexor responses and all the other reflexes were normal. His wife said that he was no longer irritable and passionate, and that his temper was equable; that in fact he was now "a different man, quite like his old self."

On May 7, 1914, he was injected with another dose of 0.9 gm. of neosalvarsan; and on June 17, 1914, his Wassermann reaction was

serum	4.4.4.0.0.
cs.f.	0.0.0.0.0.

§ 4.—*Muscular Atrophy.*

When we consider the nature of the changes produced in the spinal meninges by the activity of the syphilitic virus, it is obvious that the anterior nerve-roots must suffer, as their fibres are leaving the spinal cord. Muscular atrophy must consequently occur from time to time as a natural result of syphilis meningo-vascularis. We have already given an instance of such a lesion affecting both posterior and anterior nerve-roots, and causing loss of sensation and muscular wasting in one leg (No. 60, p. 20). Occasionally, however, the anterior roots alone are affected and, if the muscular atrophy occupies the upper extremity, it is usually spoken of as syphilitic amyotrophy.

Now the nature of muscular atrophy in syphilitic persons has been the subject of much discussion; but Léri [7] and others have amply demonstrated the existence of a progressive amyotrophy due to meningo-vascular changes of syphilitic origin.

But the cause of progressive muscular atrophy associated with signs

of tabes dorsalis stands on a less certain footing, and we shall therefore consider the views of the various authorities on syphilitic amyotrophy more fully in the chapter on syphilis centralis (p. 109). Meanwhile we give an instance characteristic of that form of muscular atrophy due to spinal meningitis and its associated vascular changes. In this patient [No. 36] other signs of active syphilis were apparent in the central nervous system, in addition to the muscular atrophy; for not only had she suffered from a prodromal headache and a "stroke," in which she lost her speech for a time, but her pupils reacted badly to light, there was slight weakness of the left half of the face, and ankle-clonus, together with an extensor plantar response, was obtained from both feet. She also had difficulty in holding her water, and could not control her motions if they were soft.

A Case of Muscular Atrophy of both Upper Extremities, with signs of Pyramidal Interference. Positive Wassermann Reaction in the Cerebro-spinal Fluid. History of previous Cerebral Affection.

Case 36.—R. C., female, married; born 1876. She was married in 1900, at the age of 24, but left her husband three years later, because he would not work. No definite history of syphilitic infection was obtained. She had never been pregnant.

In 1909 she suffered for four weeks from intense headache, which ultimately passed away entirely.

In December, 1910, she had a "stroke"; her speech became affected, and she was unable to walk steadily. Since then her memory had deteriorated, and she had been unable to work.

In January, 1912, her right hand began to waste, and she lost power so rapidly that, by June of the same year, she was unable to hold a knife. This wasting was thought at another hospital to be due to cervical ribs, and in July a rib was removed, but she steadily grew worse. In September the left hand became affected. Ever since the middle of 1912 occasionally she had been unable to control her motions or hold her water.

In November, 1912, she was admitted to the London Hospital under the care of Dr. F. J. Smith. Her speech was slurred. She suffered from no headache, and had not been subject to attacks of vomiting.

The pupils reacted to light, but the contraction was not maintained, and tended to be rhythmic; the reaction was normal on accommodation. The eyes moved well. Her face was expressionless, and there was slight weakness of the lower portion on the left side. The tongue moved well, and was not tremulous. Movements of the jaws, palate, and larynx were normal.

Smell, taste, hearing, and vision were unaffected, and the fundi showed no abnormal appearances.

All the muscles of both hands, of both forearms, and to a less degree of the arms, were considerably wasted, especially on the left side. The muscles

of the shoulder-girdle were much less affected. Both lower extremities were slightly spastic.

No hyperalgesia or loss of sensation could be discovered, even in the arms.

The knee-jerks were exaggerated, ankle-clonus was obtained on both sides, and both plantar reflexes gave an extensor response. The abdominal reflexes were unaffected.

She had considerable difficulty in holding her water, and could not control her motions if they were soft.

There was some osteo-arthritis of the right shoulder, elbow, and wrist.

No abnormal signs were discovered in the heart, lungs, or abdomen, and the urine contained neither albumen nor sugar.

On November 28, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.2.}{\text{cs.f. } 4.4.1.0.0.}$

Such a case exactly fits in with the description given by Léri [7] and Léri and Lerouge [9] of cases of muscular atrophy due to meningo-vascular changes, in two of which a microscopical examination was carried out.

But in the next case (No. 146) the signs were much less extensive; the pupils reacted well, the plantar reflexes were normal and the sphincters unaffected. The astonishing recovery under treatment and the simultaneous change in the strength of the Wassermann reaction in the cerebrospinal fluid show, however, that the case was one of syphilis meningo-vascularis amyotrophica.

A Case of Muscular Atrophy of the Right Upper Extremity with no other gross signs of Nervous Disease. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid.

Case 146.—M. S., female, married; born 1885. In July, 1910, soon after the birth of her last child, she began to lose power in the right thumb and hand; within the space of one year all the muscles of the right forearm and hand had become wasted, and she was unable to use this hand for grasping. For the first twelve months after the onset of this wasting, pain was not a noteworthy feature, but in October, 1911, she began to complain of severe pains in the back of the neck, shooting down the affected limb.

No history of syphilitic infection could be obtained; but in 1904, shortly after marriage at the age of 19, she suffered from "anæmia and indigestion." Her husband died in an Asylum of "dementia paralytica" in June, 1912. The first child of this marriage was born in 1904 and died three months later of "wasting;" the second born in 1905 survived and is healthy; the third was born in 1907 and the fourth in May, 1910. The child born in 1910 gives a negative Wassermann reaction in the serum.

On admission to the London Hospital in March, 1912, there was grave weakness and wasting of the right upper extremity. She was unable to grasp

small objects with her right hand. The right wrist was dropped and the extensor muscles of the right fingers and thumb were extremely paretic; the flexor muscles were less affected than the extensors. All the small muscles of the hand, the interossei, the thenar and hypothenar muscles, were intensely wasted. The muscles around the right shoulder-joint were fairly developed. The small muscles of the right hand and the extensor muscles of the right forearm did not react to the interrupted current; to galvanism they responded with a characteristically slow contraction. The left upper extremity was completely unaffected. Her gait was natural and her legs showed neither wasting nor spasticity.

She complained of severe dragging and shooting pains in the back of the neck and along the right forearm; but, on testing, no disturbance of sensibility could be discovered anywhere.

The knee-jerks were brisk and ankle-jerks were readily elicited. The abdominal reflexes were easily obtained and both plantar reflexes gave a flexor response.

Mentally she was depressed and worried, but her memory and attention were good. She complained of no headache and there was no tenderness of the scalp. She had suffered neither from seizures nor from attacks of vomiting.

All ocular movements were well performed. The pupils reacted briskly to light and accommodation. The face was flattened and expressionless. The tongue showed no fibrillary tremors. The movements of the palate and larynx were unaffected. Vision and the optic discs and fundi were unaffected; smell, hearing and taste were normal.

At no time had she experienced any difficulty in holding or passing her water.

On April 24, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.2.}$ and the cells numbered 10 per cubic millimetre.

On July 29, 1912, she was injected with 0.9 gm. of neosalvarsan, and on August 1 this dose was repeated. After the injections her mental state brightened, the pains in the neck ceased and power in the right upper extremity began to return.

On November 27, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.3.2.0.}{\text{cs.f. } 4.1.0.0.0.}$ and the cells numbered 20 per cubic millimetre.

On November 30, 1912, she was given another dose of 0.9 gm. of neosalvarsan.

About Christmas, 1912, she again became pregnant, and on September 20, 1913, was delivered of a healthy male child.

On December 3, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f. } 4.0.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

On December 4, 1913, she was again injected with 0.9 gm. of neosalvarsan.

In May, 1914, the extensor muscles of the right forearm had regained their normal size and power and the grasp of the right hand was as powerful as that of the left, but the muscles of the first interosseous space were still small and paretic.

Thus we agree with Léri that one form of spinal amyotrophy is certainly due to the meningo-vascular changes of syphilis; we can confirm his statements that the atrophy is liable to be accompanied or preceded by pains of root-origin, and that the reactions of the pupil may be disturbed. We also agree that there is considerable lymphocytosis in the fluid from the lumbar sac, and would add that, in these cases, the Wassermann reaction is positive in the cerebrospinal fluid if the patient has not been treated with mercury or intravenous injections of the arsenic compounds.

We believe, however, that there is another group of cases where the disease, though of syphilitic origin, progresses uninfluenced by treatment. Such a condition is exactly analogous to tabes dorsalis and will be dealt with in Chapter V, where we discuss syphilis centralis (*vide* p. 109).

§ 5.—*Myelitis.*

There is no period after infection when the patient may not be attacked with a paraplegia, showing all the symptoms and signs of a more or less complete transverse lesion of the spinal cord; this is usually spoken of as syphilitic "myelitis" or "meningo-myelitis." It is not uncommon in the secondary stage and may be accompanied by a rash upon the body and mucous patches of the mouth and anus. But an exactly similar set of signs and symptoms of intraspinal disease may appear many years after infection. From the neurological aspect, there is no obvious difference between the clinical manifestations at the different "stages." In all cases the essential signs are those of meningitis accompanied by more or less vascular disturbance.

The pathology of this "meningo-myelitis" has been fully worked out by innumerable observers (cf. Nonne [13], p. 377 *et seq.*); the lesion consists of inflammatory infiltration of the meninges and spinal nerve-roots accompanied by a variable amount of destruction of the spinal cord, secondary to a disturbance of its blood-supply. It is in fact a characteristic meningo-vascular condition.

Perhaps the commonest clinical manifestations produced by such a lesion are spastic paralysis, with or without a girdle sensation; spasticity with ataxy is also extremely frequent and occasionally this variety of the disease produces a more or less perfect form of Brown-Séquard paralysis. But in this case the signs of pyramidal affection are always bilateral, however completely the sensory manifestations may follow the Brown-Séquard type.

In cases of "meningo-myelitis" micturition tends to be disturbed early in the course of the disease, and some difficulty in passing the water may form one of the earliest symptoms (cf. No. 19, p. 27).

The cerebrospinal fluid from these patients tends to yield an extremely positive Wassermann reaction; but this can usually be profoundly affected by treatment. Thus in No. 134 and also in No. 10, who had been under treatment previously with mercury, it became entirely negative.

The final result, however, from the patient's point of view, depends on the amount of secondary destruction of tissue which has occurred in consequence of vascular occlusion or diminished blood-supply.

A Case of so-called "Myelitis," with a Positive Wassermann Reaction in the Cerebrospinal Fluid, which became greatly reduced in strength within Four Months of Treatment.

Case 134.—G. R., male, married, naval tailor; born 1874. This patient joined the Navy at the age of 21, and remained in good health until he caught syphilis in October, 1910, at the age of 36. He suffered from a chancre on the penis, which was followed by the development of adenitis, anæmia, a rash, and condylomata. He was treated at the Royal Naval Hospital, Chatham, with eight injections of mercury, and then took mercurial pills for fourteen months until January, 1912.

On January 6, 1912, after a period of ill-health, in which he complained chiefly of headaches and giddiness, he had a seizure which was followed by the development of a right-sided hemiparesis. On January 9, 1912, he was admitted to the Chatham Hospital, and was treated with mercury and iodides by the mouth. On March 7, 1912, he was discharged from hospital apparently cured.

On June 1, 1912, the left leg became affected; this was followed by retention of urine, pains in the back and abdomen, and later by a complete inability to move both legs.

On June 13, 1912, he was admitted to the London Hospital. The general aspect of the patient somewhat resembled that of a case of congenital syphilis. The nasal bridge was greatly depressed, the hair was receding, but the teeth were not pegged, and no scars were seen around the angles of the mouth. Pigmented scars were present on the front of both shins, and there was a scar on the penis.

His attention and memory were impaired. He complained of intense general headache, accompanied by pressure tenderness of the scalp and of dreams and "frights" by night. He had suffered from a seizure on January 6, 1912, but had not been subject to attacks of vomiting. His speech was slurred and mentation slow. Vision and the fundi were unaffected. He was deaf in both ears; tests showed that both internal ears were affected, the right more so than the left. Smell and taste were normal.

All movements of the eyeballs were badly performed, but there was no actual paralysis of any external eye-muscle. The pupils were equal, and reacted normally. The other cranial nerves were unaffected.

He could just move both legs; the power at the right hip was greater than that at the left; he could not move the toes or ankles either on the right or on the left side. In action the hands were clumsy and paretic, and the grasps were feeble. Alignment of the fingers was defective; closure of the eyes caused the outstretched hands to fall away, and diminished the power of his grip. The lower abdominal muscles and the lower portion of the erector spinæ were completely paralysed. All the muscles below the umbilicus were flaccid.

All forms of sensibility were gravely defective below the level of the distribution of the eighth thoracic roots on both sides. Sensation to light touch, and to heat, cold, and pain were impaired, but nowhere completely lost. He could not appreciate the vibrations of a tuning-fork below the level of about the ninth ribs, and was unable to recognize posture and passive movements in both legs. Over both upper extremities sensibility to touch, pain, and temperature was not impaired, but recognition of posture and passive movement was poor, and the length of time during which the vibrations of the tuning-fork were appreciated was relatively shortened.

The right knee-jerk was extremely brisk, the left was readily obtained. Ankle-clonus could not be elicited. On both sides the plantar reflexes gave an extensor response. The abdominal and cremasteric reflexes were completely abolished. The wrist- and elbow-jerks were obtained.

He was unable to pass urine, and suffered from retention with overflow. This was complicated with a stricture of the urethra and cystitis. The Wassermann reaction on June 19, 1912, was $\frac{\text{serum 4.4.4.4.0.}}{\text{cs.f. 4.4.4.4.4.}}$

He was given 0.6 grm. of salvarsan on June 28, 1912, and 0.9 grm. of neosalvarsan on July 21, 1912, and on October 8, 1912; on the last date the Wassermann reaction was $\frac{\text{serum 4.2.1.0.0.}}{\text{cs.f. 4.2.0.0.0.}}$

On July 19, 1914, he was readmitted to the Hospital. The physical signs were little altered but his general condition was greatly improved, and he could now do his work as a tailor,

On July 22, 1914, the Wassermann reaction was $\frac{\text{serum 2.0.0.0.0.}}{\text{cs.f. 0.0.0.0.0.}}$ and the cells numbered 2 per cubic millimetre.

A Case of Brown-Séquard Paralysis where a Positive Wassermann Reaction in the Cerebrospinal Fluid became Negative under Treatment.

Case 10.—C. B., male, single, pawnbroker's assistant; born 1870.

He denied all venereal infection; but in August, 1908, a typical gumma of the forearm appeared and healed rapidly on the administration of iodides.

On June 1, 1911, he began to complain of tightness across the upper abdomen. The pains continued off and on until August 17, 1911, when he found that he could not pass his water; complete retention of urine developed,

necessitating the use of a catheter, and on August 21, 1911, he was admitted to the London Hospital.

On admission he complained of boring pains in the head accompanied by pressure tenderness of the skull. His mental state was little affected. Speech was natural. He had never complained of vomiting. No abnormal signs were discovered in the territory of the cranial nerves.

There was complete flaccid paralysis of the left leg and grave weakness of the right. The arms were unaffected.

He complained of spontaneous shooting pains in the upper part of the chest on both sides over the areas supplied by the third to the sixth thoracic nerve-roots and over this region of the trunk hyperalgesia was present to the dragged point of a pin. Below the hyperalgesic zone on both sides there was much loss of sensation to the prick of a pin, painful pressure, and to the hot and cold tubes. This loss was greater on the right leg than on the left. To passive movement and the vibration of a tuning-fork there was also considerable loss of sensibility, greater on the left leg than on the right. Appreciation of touches with cotton-wool was less affected on both legs than any other form of sensibility.

The knee-jerks on both sides were exaggerated, more so on the left than on the right. Ankle-clonus was readily obtained on the left side and was less definite on the right. The plantar responses on both sides were extensor. The lower abdominal reflexes could not be elicited, the upper ones were brisk. The wrist- and elbow-jerks were normal.

There was complete retention of urine with overflow and an inability to hold the motions when soft.

Between August 28 and October 4, 1911, he was treated with thirty-six inunctions of mercury and the weakness of the legs improved rapidly.

On June 6, 1912, the Wassermann reaction was $\frac{\text{serum 4.4.4.1.0.}}{\text{cs.f. 4.1.0.0.0.}}$

On July 22, 1912, he was injected with 0.6 gm. of salvarsan, and on July 27, 1912, with 0.9 gm. of neosalvarsan.

On July 2, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.1.0.}}{\text{cs.f. 0.0.0.0.0.}}$ and the cells numbered 1 per cubic millimetre.

On June 28, 1913, he was again injected with 0.9 gm. of neosalvarsan, and on December 4, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.0.0.0.}}{\text{cs.f. 0.0.0.0.0.}}$ and the cells numbered 2 per cubic millimetre.

Since November, 1911, his physical condition has remained stationary. In January, 1914, he showed spastic paralysis of the left leg, with profound loss of appreciation of vibration and of posture. Sensibility to pain, heat and cold was greatly diminished over the right lower extremity. But, like so many of these cases of Brown-Séquard paralysis of syphilitic origin, ankle-clonus could be obtained on both sides and both plantar reflexes gave an extensor response. His sphincters were controlled with difficulty.

§ 6.—*Lateral and Combined Degenerations.*

Not infrequently meningo-vascular syphilis produces clinical manifestations closely resembling those due to primary degeneration of the long tracts of the spinal cord. The patient suffers from spasticity, with or without ataxy, and no girdle sensation or root-area is present to indicate the focal level of the lesion. But such cases differ from those of primary degeneration of the lateral and posterior columns of the spinal cord in the effect produced by treatment on the positive Wassermann reaction in the cerebrospinal fluid. From strongly positive it may become negative, and at the same time the symptoms may improve considerably; but as the essential lesion is frequently a secondary degeneration, consequent on slow vascular occlusion, the improvement is less than in many cases of apparently severe "meningo-myelitis."

We have chosen No. 91 to illustrate this condition because, in addition to the signs of interference with the pyramidal tracts, he had an area of radicular hyperalgesia and transitory difficulty in micturition, showing that the lesion in these cases is closely akin to that in "meningo-myelitis."

He also illustrates remarkably well the change that can be produced in the Wassermann reaction of the cerebrospinal fluid by effective treatment.

A Case of "Meningo-myelitis" accompanied by a Gumma of the Palate. Positive Wassermann Reaction in the Cerebrospinal Fluid which became Negative under Treatment. Appearance of Herpes Zoster over the Second Cervical Area.

Case 91.—D. K., male, married, labourer; born 1878. In 1904, at the age of 26, he contracted syphilis and suffered from a chancre, rash and sore throat, for which he was treated with mercury by the mouth for twelve months.

In 1907 he developed gummatous ulcers on his shins which healed rapidly on the administration of iodides.

On January 4, 1912, he was taken ill with dizziness, pains in his abdomen and repeated vomitings. This attack was followed by headache, which lasted until his admission in July, 1912.

About four weeks before his admission a pimple appeared on his palate which enlarged, broke down and led to a perforation into the nose.

On admission to the London Hospital in July, 1912, all the cerebral functions were unimpaired; speech and memory were unaffected. He had not suffered from seizures but complained of severe, general, gnawing pains in the head accompanied by soreness of the scalp and tenderness on pressure. The pains were constantly present, but were always worse at night. From time to time before admission he had suffered from attacks of retching,

flatulence, abdominal distension, pyrosis and even actual vomiting. The special senses were unaffected.

Movements of the eyes, face, tongue, palate and larynx were unimpaired, and the pupils reacted normally.

He walked well and was not ataxic. Both great toes tended to remain in the extended posture, although there was no noticeable increase of tone in the muscles of the lower extremities, and no loss of muscular power.

Distinct tenderness and hyperalgesia were present in the region of the eighth and ninth thoracic nerve-roots on both sides, but no sensory change could be discovered elsewhere to any test.

The knee-jerks and ankle-jerks were exaggerated and both plantars gave an extensor response. The upper abdominal reflexes were brisk and the lower ones could just be obtained.

He had a little difficulty in beginning micturition, but no other sphincter trouble.

A small perforation was seen at the back of the hard palate leading from the mouth to the nose. No abnormal signs were discovered in the heart, lungs, abdomen or urine.

On July 10, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.3.0.0.}{\text{cs.f. } 4.4.4.1.0.}$

He was given 0.6 gm. of salvarsan on July 10, 1912, and a similar dose on the 17th. By January 15, 1913, the reaction had become $\frac{\text{serum } 3.2.1.0.0.}{\text{cs.f. } 1.0.0.0.0.}$. At the same time the headache and the hyperalgesia around the trunk disappeared and his general condition improved strikingly.

On January 15, 1913, he was given 0.9 gm. of neosalvarsan. To this dose there was no provocative increase in the strength of the Wassermann reaction in the serum, for on January 22, 1913, the reaction was $\frac{\text{serum } 3.2.1.0.0.}{\text{cs.f. } -. -. -. -.}$ and this remained at about the same strength until June, 1913. On June 6, 1913, the reaction was $\frac{\text{serum } 3.2.1.0.0.}{\text{cs.f. } -. -. -. -.}$. When, however, this patient was seen on June 25 he showed a typical herpetic eruption on the supply of the second cervical root, on the right side, and at the same time the reaction had increased to $\frac{\text{serum } 4.3.0.0.0.}{\text{cs.f. } -. -. -. -.}$. At this time he received no further anti-syphilitic treatment and yet on August 26, 1913, the reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -. -. -. -.}$ but on November 12, 1913, it had again risen to $\frac{\text{serum } 4.1.0.0.0.}{\text{cs.f. } -. -. -. -.}$ without the appearance of any fresh manifestations.

§ 7.—*Epilepsy.*

It is generally recognized that diffuse changes in the cerebral meninges of syphilitic origin may produce a condition indistinguishable

from idiopathic epilepsy. We are not concerned here with a localized gummatous meningitis and its Jacksonian attacks, but with a more diffused lesion associated with recurrent loss of consciousness and general convulsions (cf. Nonne [13], p. 141).

It is obvious that idiopathic epilepsy may occur in a man who has been affected with syphilis and yet the two conditions may not be in any way connected pathologically. But, on the other hand, there can be little doubt that a condition, clinically indistinguishable from epilepsy, may occur as the direct result of syphilis. With a positive Wassermann reaction in the serum and a negative one in the cerebrospinal fluid, it is, however, impossible to be certain of such a diagnosis unless some other physical sign points to the organic nature of the lesion.

We have, therefore, chosen No. 303 and No. 207 as our examples, because in both cases the defective reaction of the pupils pointed to something more than idiopathic epilepsy. At the same time the negative reaction in the cerebrospinal fluid makes it unlikely that they are instances of Fournier's "parasyphilitic epilepsy" ([4], p. 238), or, as we should prefer to call it, syphilis-centralis with epileptiform attacks (*vide* Chapter V, § 6, p. 121).

Both these patients illustrate the general mental disturbance so commonly associated with attacks of syphilitic epilepsy. Thus in No. 303 the first seizure was followed by a period of confusion lasting at least twenty-four hours, and No. 207 usually remains "dazed" for many hours after waking from his post-convulsive sleep. He also illustrates the extreme difficulty in preventing the fits by means of bromides; this drug somewhat diminishes the severity and frequency of the attacks, but does not produce that improvement we should expect in a case of idiopathic epilepsy.

A Case of Epileptiform Convulsions, associated with Defective Reaction of the Left Pupil and Loss of the Ankle-jerks. Negative Wassermann Reaction in the Cerebrospinal Fluid.

Case 303.—A. S., male, single, tramcar driver; born 1879. In 1900, at the age of 21, he contracted syphilis and suffered from a sore on the penis and a discharge from the urethra which were followed by a bubo in the right groin, but no manifestations of secondary syphilis; he was treated for a few weeks only.

Early in 1911 he became very sleepy; after driving his tram for some time he would come home and immediately fall asleep; whilst driving he often felt sleepy, but never actually fell asleep on the car. Shortly after this he became subject to severe headaches.

On January 17, 1912, about 7 p.m., he was in charge of his car when he

ran into a barrow; he just touched the barrow, but no damage was done. Fifteen minutes later he "came over dazed," stopped the car and immediately fell forward. He was taken to the London Hospital and admitted in a dazed, semi-conscious condition; he could hardly speak and misused words; he moaned and wept bitterly. On his arrival in the ward he was excited, restless and difficult to manage. He remained an in-patient until January 19, 1912, and on discharge seemed perfectly normal. No gross manifestations of disease were discovered.

He then remained in fair health until June, 1912, when he had an epileptiform attack in the street, lost consciousness and was carried home; an hour later he came to himself. He was then free from seizures until December, 1912; on the 15th of that month whilst sitting reading in front of the fire he lost consciousness and fell into the fireplace. The fourth attack occurred in September, 1913; he was walking in the street about 7 p.m. when he was seized with a sharp shooting pain in the head; he felt drowsy, sat down on the pavement and then "struggled" and lost consciousness. Between September, 1913, and January, 1914, when he first came under our observation, he had four or five small fits. On January 20, 1914, an attack came on without warning and was much more severe and lasted much longer; he was unconscious for two hours, became extremely violent, was cyanosed, bit his tongue and passed his water. On February 20 he had a slight attack.

He stated that since his first seizure his memory had become defective. In 1912 he had been subject to attacks of headache, but he had never vomited nor experienced any feelings of nausea. At no time had he suffered from any pains in the extremities or trunk. He had not lost his skill with his hands and motion had never been affected.

On his admission to the London Hospital on March 16, 1914, his mental state was unaffected, his attention good. He slept normally. Memory to ordinary tests was unaffected and no suggestions of dementia were present.

His speech was natural, and hearing, smell, taste and vision normal. The optic discs and fundi appeared healthy. All ocular movements were well carried out. The pupils were equal, well centred, and regular in outline; the left pupil did not react to light but reacted well to accommodation, the right reacted briskly both to light and to accommodation. The expression of his face was normal. Movements of the jaw, palate, larynx and tongue were unimpaired. Motion, sensation and the action of the sphincters were completely unaffected. The knee-jerks were natural, but both ankle-jerks were abolished. The wrist- and elbow-jerks were normal and the abdominal reflexes brisk. Both plantar reflexes gave a flexor response. No abnormal signs were discovered in heart, vessels, lungs, abdomen or urine.

On March 18, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre. He was injected with doses of 0.9 grm. of neosalvarsan on March 18, March 20, and March 22, 1914. On April 22, 1914, he had a slight fit, and since that time has remained free from attacks (July, 1914), and his general health has improved greatly.

A Case of Epileptiform Seizures with Defective Reaction of the Pupils. Negative Wassermann Reaction in the Cerebrospinal Fluid.

Case 207.—F. W., male, married, labourer; born 1871. In 1892, at the age of 21, this patient contracted a hard chancre, followed by recurrent sore throat, fall of hair and anæmia; he was treated with mercury by the mouth for two years.

In 1897 he married. His first child, born in June, 1897, gives a positive Wassermann reaction in the serum, and shows the characteristic features of congenital syphilis. Five miscarriages followed this pregnancy; the next living child was born in 1903, and children born in 1908 and 1912 also survive.

After marriage he drank heavily. During the years 1901, 1902 and 1903 he was constantly ailing; he complained chiefly of his head, due, as he thought, to alcoholic excess. One hot day in June, 1903, whilst at work on a scaffold, he was seized with a severe left-sided headache, and about half an hour later had his first "fit." In this attack he lost consciousness and wetted himself. After this he suffered from a severe dull headache and completely lost his sense of taste. At this time he was in bed for seven days and away from work for a fortnight. From July, 1903 until the beginning of 1905 he attended the London Hospital as an out-patient and was treated with bromides for "epilepsy." At first the fits came on about once a week, but under treatment the frequency and severity of the attacks diminished. About October, 1904, he began to complain of attacks of pain in the chest, "a tightness and a feeling as if knives were being inserted into the skin." From October, 1904, until January, 1905, he had an attack of this sort almost every day. In the years 1906, 1908 and again in 1912 he suffered from "shooting rheumatic pains" in the back of the thighs and the inner side of the legs and feet. In 1911 he ceased to take bromides and gradually the fits became more severe and more frequent. In 1912 he also complained at various times of pains shooting down the inner side of the right arm and forearm, and in the right axilla, and later in the same year was much troubled with "sciatica" in the back of the thighs and calves. From time to time between the years 1895 and 1913 he complained of "soreness of the mouth with ulceration."

The fits were characteristically epileptiform. They came on at any time by day or night. Usually a seizure occurred about once a fortnight, but frequently the attacks would come on in groups of three or four. Before the seizure he felt "full and muzzy," and he knew that a fit was hanging about him because he lost his taste. In each attack he became unconscious and cyanosed; he usually passed his water and frequently bit his tongue. In the attack he said that he "felt a sort of pain creeping up the limbs, more especially on the right side, then a tingling in the left eye and the left side of the face, next his sight became dim, he heard distant noises in his ears and then he lost himself." In the attacks, which occurred whilst he was under observation, his head was seen to turn to the left and, before the convulsion became generalized, he closed his left fist tightly. After the

attacks he was dazed and drowsy for some hours, and, if alone, usually slept. He said that alcoholic excess would always bring on the fits, and that they occurred more frequently when he was worried or away from work.

He complained of attacks of headache in the frontal and vertical regions passing into the back of the neck; when the headache came on the vision of the left eye was always affected. In 1903 he had been subject to attacks of nausea and vomiting, but after that year he rarely vomited.

On admission to the London Hospital in June, 1913, his speech was slow and his articulation defective, but there was no slurring of syllables. His memory was bad. He did not know the year of his birth and could not calculate back to the date of his marriage. He knew the value of money, but had forgotten his multiplication tables. He was unable to remember any details of events which had happened more than a few weeks before his admission. Mentation was slow, but his answers to questions were accurate and rational. He was nervous, irritable and inattentive. He boasted freely, but had no grandiose ideas. Delusions and hallucinations were absent.

Hearing was not affected, smell was poor and before each fit he completely lost all sense of taste; this returned in part after the attack had passed off. Vision and the visual fields were not grossly affected, and the optic discs and fundi appeared natural.

All ocular movements were well performed. The pupils were small, well centred and regular in outline; neither reacted to moderate illumination, but both reacted sluggishly to strong lights and well to accommodation. The movements of the face, jaws, palate and tongue were unaffected. The gait was natural and all co-ordinated movements were well carried out.

He complained of no spontaneous pains, but over the front and back of the chest, within an area corresponding to the distribution of the third, fourth, fifth, and sixth thoracic roots on both sides, pricks were said to be "less sharp" and "less localized," and the sensation evoked by the hot and cold tubes seemed "less hot" or "less cold" than elsewhere over the body. To pinching of the skin and the dragged point of a pin the skin around the right shoulder-joint was tender. There was no sensory loss to posture, passive movement, the vibrations of a tuning-fork, cotton-wool, heat and cold elsewhere on the extremities or trunk.

Osteo-arthritic grating was present in the right shoulder-joint and the patient complained of pain when this joint was moved.

The knee- and ankle-jerks, and the abdominal and plantar reflexes all gave normal responses, and the sphincters were controlled.

The tongue was deeply fissured and a scar was present on the penis. The teeth were notched and much worn, the nasal bridge was depressed but no scars were seen at the angles of the mouth.

No abnormal signs were discovered in the heart, lungs, abdomen or urine.

On June 6, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.3.0.}}{\text{cs.f. 0.0.0.0.}}$ and the cells numbered 2 per cubic millimetre.

On June 13, June 19 and June 26, 1913, he was injected intravenously with doses of 0.9 gm. of neosalvarsan. After the first two of these injections he had three epileptiform attacks exactly resembling those described above.

[B] THE WASSERMANN REACTION IN SYPHILIS MENINGO-VASCULARIS.

It was generally held that the cerebrospinal fluid gave a negative reaction in syphilitic affections of the central nervous system, and that this was an important aid in differential diagnosis between such conditions and "parasyphilis," where the reaction was overwhelmingly positive. This view was expressed by Plaut as late as 1913 [19] and by Mott in his first communication to the International Medical Congress [11]; subsequently, however, Mott somewhat modified his statement, [12]. In 1912 Nonne stated that the cerebrospinal fluid is not usually positive except with the larger volume of fluid used in the "Auswertungsmethode" of Hauptmann and Hössli; then, however, it is always positive. Later, before the International Medical Congress in 1913, Nonne [14] summed up his views on this subject in the following statement: "Auch das Verhalten der W.-R. bei Tabes und Paralyse und bei den atypischen syphiligen Rückenmarkserkrankungen lässt seit der Einführung der Hauptmannschen Auswertungsmethode einen *prinzipiellen* Unterschied gegenüber den echtluetischen Erkrankungen des Nervensystems nicht erkennen."

But early in this research [10] we were led to believe that the character of the Wassermann reaction in the cerebrospinal fluid, in cases of meningo-vascular syphilis, depended mainly on the site of the lesion. If the signs and symptoms pointed to an affection of the spinal cord, its membranes or nerve-roots, the reaction was usually positive in the cerebrospinal fluid, and the strength of this reaction was often as great as that in any other condition of syphilitic origin.

But the more completely the clinical manifestations were confined to some affection of the cerebrum or its vessels, the more often was a negative reaction obtained in the cerebrospinal fluid. Even when a positive reaction was present, it was relatively feeble and usually transitory.

Between the cerebrum on the one hand and the spinal cord on the other stands the behaviour of the reaction with affections of the cranial nerves, produced by meningo-vascular syphilis. Sometimes the cerebrospinal fluid gives a positive, sometimes a negative reaction, according to the extent and situation of the signs and symptoms [cf. p. 49].

INCIDENCE OF THE WASSERMANN REACTION IN SYPHILIS MENINGO-VASCULARIS.

TABLE A.—Cases in which the Contents of the Spinal Canal were apparently affected.

No. of case	Result of first examination	No. of case	Result of first examination
3 (p. 34)	serum 4.4.4.4.4. cs.f. 4.4.4.3.2.	175	serum 4.4.4.4.4. cs.f. 4.4.4.4.2.
10 (p. 71)	4.4.4.1.0. 4.1.0.0.0.	177	4.4.4.4.4. 4.4.4.4.0.
19 (p. 27)	4.4.4.4.4. 4.4.4.3.2.	189 (p. 60)	4.4. - - - 4.4.4.0.0.
26	4.4.4.4.4. 4.4.4.0.0.	201	4.4.4.4.4. 4.4.4.4.4.
36 (p. 66)	4.4.4.4.2. 4.4.1.0.0.	202	4.4.4. - - 4.3.0.0.0.
45	4.4.4.4.4. 4.4.4.4.4.	217	4.4.4.4.0. 4.4.4.4.0.
59 (p. 37)	4.4.4.4.4. 4.4.4.4.3.	226 (p. 46)	4.4.4.4.1. 4.4.3.0.0.
60 (p. 20)	4.4.4.4.4. 4.4.3. - -	228	4.4.4.4.4. 1.0.0.0.0.
64	4.3.2.0.0. 4.4.4.3.1.	235	4. - - - - 4.4.2.0.0.
74 (p. 51)	4.4.4.4.3. 4.4.4.3.1.	236	4.4.4.4.2. 0.0.0.0.0.
77	4.4.4.4.4. 4.4.4.3.0.	237	4.4.4.4.3. 4.4.4.4.4.
86 (p. 44)	4.4.3.3.0. 4.4.4.4.0.	239	4.4.4.4.0. 4.4.2.0.0.
91 (p. 73)	4.4.3.0.0. 4.4.4.1.0.	244	4.4.4.3.0. 4.4.4.0.0.
94	1.0.0.0.0. 4.4.4.3.0.	255	4.4.4.1.0. 4.4.4.0.0.
102	4.4.0.0.0. 4.3.1.0.0.	256	4.4.4.4.1. 4.4.4.4.4.
106	4.4.4.4.4. 4.4.0.0.0.	262 (p. 62)	4.4.4.4.4. 4.4.4.4.0.
114	4.2.0.0.0. 4.4.4.4.4.	273	4.4.4.4.3. 4.4.4.4.4.
134 (p. 70)	4.4.4.4.0. 4.4.4.4.4.	277	4.4.4.4.4. 4.4.4.4.4.
146 (p. 67)	4.4.4.4.4. 4.4.4.4.2.	279	4. - - - - 4.4.4.4.4.
147 (p. 22)	0.0.0.0.0. 4.4.1.0.0.	284 (p. 11)	4.4.4.4.4. 4.4.4.4.0.

No. of case	Result of first examination	No. of case	Result of first examination
296	serum 4.4.4.3.0. cs.f. 4.1.0.0.0.	309 (p. 32)	serum 4. - - - cs.f. 4.4.4.0.0.
305	4.4.4.4.4. 4.4.4.3.1.	313 (p. 30)	4.4.4.4.4. 4.4.0.0.0.
308	4.4.4.4.4. 4.0.0.0.0.		

TABLE B.—Cases in which the Intra-cranial Contents only were affected.

11	serum 4.4.4.4.0. cs.f. 0.0.0.0.0.	170	serum 4.4.4.4.4. cs.f. 4 4.0.0.0.
15	4.4.4.4.0. 0.0.0.0.0.	204	4.4.4.4.1. 0.0.0.0.0.
39	4.4.4.4.4. 0.0.0.0.0.	205	4.1.0.0.0. 0.0.0.0.0.
53 (p. 40)	4.4.4.0.0. 0.0.0.0.0.	207 (p. 77)	4.4.4.3.0. 0.0.0.0.0.
62	4.4.2.0.0. 0.0.0.0.0.	223	4.4.4.4.4. 0.0.0.0.0.
73	4.4.4.4.0. 0.0.0.0.0.	232	4.4. - - - 0.0.0.0.0.
92 (p. 57)	4.4.4.4.0. 0.0.0.0.0.	240 (p. 48)	4.4.4.4.4. 0.0.0.0.0.
104	4.4.4.4.3. 0.0.0.0.0.	253 (p. 53)	4.4.4.4.4. 4.4.0.0.0.
107	4.4.3.1.0. 4.2.0.0.0.	269	4.4.1.0.0. 0.0.0.0.0.
110	0.0.0.0.0. 0.0.0.0.0.	271 (p. 41)	4.4.4.4.2. 0.0.0.0.0.
111	4.3.1.0.0. 0.0.0.0.0.	287	4.4.3.0.0. 0.0.0.0.0.
122 (p. 16)	4.4.4.4.4. 0.0.0.0.0.	289	4.3.0.0.0. 0.0.0.0.0.
128 (p. 56)	4.4.4.4.4. 4.1.0.0.0.	290	4.4.4.0.0. 0.0.0.0.0.
133	4.4.4.4.4. 0.0.0.0.0.	303 (p. 75)	4.4.4.2.0. 0.0.0.0.0.
149 (p. 58)	4.4.4.4.2. 0.0.0.0.0.	310 (p. 54)	0.0.0.0.0. 4.1.0.0.0.
158	4.4.4.4.4. 0.0.0.0.0.		

JUVENILE.

No. of case	Result of first examination	No. of case	Result of first examination
21	serum 4.4.4.4.4. cs.f. 3.0.0.0.0.	85	serum 4.4.4.4.4. cs.f. 0.0.0.0.0.
61	4.4.4.4.4. 0.0.0.0.0.	156	4.4.4.4.2. 0.0.0.0.0.
65	4.2.0.0.0. 0.0.0.0.0.		

But in order to show that this statement is, in the main, correct, every patient must be examined thoroughly on more than one occasion, and if possible by more than one observer. For an obvious cerebral lesion, which would not usually produce a positive reaction in the cerebrospinal fluid, may be complicated by a comparatively insignificant affection of the spinal meninges or roots; this will tend to induce a positive reaction, which, if unrecognized, may spoil an otherwise conclusive series of observations.

Even when care is taken in each case to note whether the parts within the spinal canal are affected or not, the signs are not of equal value in foretelling the probable nature of the Wassermann reaction. For in patients with cerebral syphilis signs may appear pointing to some affection of the spinal meninges so transitory and slight that we could scarcely expect them to affect the cerebrospinal fluid drawn from the lower end of the lumbar sac. It is, however, remarkable how often such indications of some spinal affection influence the reaction of the cerebrospinal fluid.

In a few instances, however, in spite of the strictest clinical examination, no signs could be discovered apart from those of disease of the cerebrum and its vessels, although the reaction was positive in the cerebrospinal fluid. But we must remember that in the Wassermann reaction we possess a means of investigation more delicate than any clinical method. On comparing the following tables, therefore, it is not surprising that they should contain exceptions to the rules we have laid down; the wonder is rather that in so many instances the clinical results should have coincided so closely with those of the Wassermann reaction.

Table A contains forty-five cases of meningo-vascular syphilis, where the clinical signs pointed to some affection of the spinal cord or its membranes, and in one only was the cerebrospinal fluid com-

pletely negative. This was the case of a young married woman (No. 236), who suffered from a meningo-myelitis below the level of the third thoracic segment. At the same time she bore the scars of gummatous ulcers on her shins, and belonged to the clinical group, in which a positive reaction is usually obtained in the cerebrospinal fluid.

Another case (No. 228) yielded so slight a reaction in the cerebrospinal fluid that it also should be classed as an exception; but as Fildes and McIntosh ([3], p. 228) pointed out, these faintly positive reactions may have no specific significance, or they may represent the last traces of a positive reaction in a fluid which is becoming negative. No. 228 subsequently developed root-lesions, and we were therefore obliged to include him under this heading; although at the time the first Wassermann reaction was obtained there were no definite signs pointing to an affection of the spinal meninges or vessels.

When we turn to Table B, containing thirty-six cases of cerebral lesions, the exceptions are more numerous; for it is much easier to obtain clinical evidence that the spinal contents are affected than to prove the opposite during life. It will therefore be well to consider more in detail these exceptional cases with a positive reaction.

No. 128 and No. 253 were both instances of cranial nerve paralyses, and, as we have already pointed out (p. 49), syphilis meningo-vascularis of the brain-stem is not infrequently associated with a positive reaction in the cerebrospinal fluid. Indeed, it is difficult to see how extensive basic meningitis could exist without some affection of the spinal meninges. In No. 128, a case of third nerve paralysis, the positive reaction became negative in the cerebrospinal fluid within six weeks of treatment. No. 253 was an instance of widespread signs of affection of many cranial nerves. Such patients usually give a positive reaction in the cerebrospinal fluid (*vide* p. 50).

In the same way, No. 107, although a case of left hemiplegia, showed some affection of the movements of the right half of the tongue, pointing in all probability to a meningo-vascular lesion of the brain-stem. To the same group belongs No. 310, an instance of Weber's syndrome; he suffered from complete paralysis of the left third cranial nerve with ptosis and a fixed pupil associated on the right half of the body with a hemiplegia of the arm and leg. Here also the reaction was a weak one, as is usual in those cases of meningo-vascular disease of the brain-stem, which give a positive reaction in the cerebrospinal fluid.

Thus, out of the five cases of cerebral syphilis, which gave a positive

reaction, four were suffering from some disease of the brain-stem, or its membranes, a condition liable to be associated with a weakly positive reaction in the cerebrospinal fluid.

Finally, in No. 170, a married woman suffering from right hemiplegia and dysarthria, we were unable, after careful examination in hospital, to find any signs of a lesion of the meninges and vessels of the spinal cord or brain-stem. In this case clinical methods failed to explain an apparent exception to our usual experience of the behaviour of the Wassermann reaction in the cerebrospinal fluid.

Of the five cases of juvenile syphilis of the brain, one yielded a weakly positive reaction, whilst all the others were completely negative.

Thus we have been able to show that in the case of meningo-vascular syphilis the key to the Wassermann reaction in the cerebrospinal fluid lies in the presence or absence of inflammatory changes in the meninges of the spinal cord and brain-stem. If they are affected, the reaction is positive, whilst, if they have escaped, the cerebrospinal fluid reacts negatively. Moreover, we have shown that in most cases careful clinical observation is able to detect signs which point to this affection of the meninges, and so enables us to foretell the character of the Wassermann reaction in the cerebrospinal fluid.

[C] THE EFFECT OF TREATMENT ON THE WASSERMANN REACTION IN SYPHILIS MENINGO-VASCULARIS.

Throughout the first part of this chapter we have insisted on the change in the Wassermann reaction of the cerebrospinal fluid which may be brought about in cases of meningo-vascular syphilis as the result of treatment, and we have described many instances where a strongly positive reaction became negative in the cerebrospinal fluid. But in order that this evidence may have its full value we have gathered together on Table C eighteen cases where the cerebrospinal fluid ultimately yielded a negative Wassermann reaction as the result of treatment. Fourteen of these cases have been fully described in the text on the page appended to the number in the first column.

In most cases this change was effected by three doses of 0.9 grm. of neosalvarsan, but in a few instances even relatively smaller doses of salvarsan were used. In all cases potassium iodide was given almost continuously throughout the period between the two Wassermann determinations.

TABLE C.—TO SHOW THE EFFECT OF TREATMENT ON THE WASSERMANN REACTION IN SYPHILIS MENINGO-VASCULARIS.

No. of case	Before treatment	After treatment	Intervening period	Nature of treatment
3 (p. 34)	<u>4.4.4.4.4.</u> 4.4.4.3.2.	<u>4.4.4.4.1.</u> 0.0.0.0.0.	30 weeks	3 doses of 0.9 grm. of neosalvarsan intravenously.
10 (p. 71)	<u>4.4.4.1.0.*</u> 4.1.0.0.0.	<u>4.4.4.1.0.</u> 0.0.0.0.0.	55 "	1 dose of 0.6 grm. of salvarsan and 1 dose of 0.9 grm. of neosalvarsan intravenously.
19 (p. 27)	<u>4.4.4.4.4.</u> 4.4.4.3.2.	<u>4.4.4.4.3.</u> 0.0.0.0.0.	41 "	1 dose of 0.9 grm. and 1 of 0.6 grm. of neosalvarsan intravenously.
59 (p. 37)	<u>4.4.4.4.4.</u> 4.4.4.4.3.	<u>4.4.1.0.0.</u> 0.0.0.0.0.	21 "	4 doses of 0.9 grm. of neosalvarsan intravenously.
60 (p. 20)	<u>4.4.4.4.4.</u> 4.4.3. - -	<u>4.4.4.4.4.</u> 0.0.0.0.0.	49 "	2 doses of 0.4 grm. of salvarsan intravenously.
74 (p. 51)	<u>4.4.4.4.3.</u> 4.4.4.3.1.	<u>4.4.4.3.0.</u> 0.0.0.0.0.	27 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
86 (p. 44)	<u>4.4.3.3.0.</u> 4.4.4.4.0.	<u>4.4.4.4.4.</u> 0.0.0.0.0.	86 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
91 (p. 73)	<u>4.4.3.0.0.</u> 4.4.4.1.0.	<u>3.2.1.0.0.</u> 1.0.0.0.0.	27 "	2 doses of 0.6 grm. of salvarsan intravenously.
94	<u>1.0.0.0.0.</u> 4.4.4.3.0.	<u>1.0.0.0.0.</u> 0.0.0.0.0.	25 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
106	<u>4.4.4.4.4.</u> 4.4.0.0.0.	<u>0.0.0.0.0.</u> 0.0.0.0.0.	24 "	2 doses of 0.6 grm. of salvarsan intravenously.
120 (p. 89)	<u>4.2.0.0.0.</u> 4.3.2.0.0.	<u>0.0.0.0.0.</u> 0.0.0.0.0.	35 "	1 dose of 0.6 grm. of salvarsan intravenously.
134 (p. 70)	<u>4.4.4.4.0.</u> 4.4.4.4.4.	<u>2.0.0.0.0.</u> 0.0.0.0.0.	109 "	1 dose of 0.6 grm. of salvarsan and 2 doses of 0.9 grm. of neosalvarsan intravenously.
146 (p. 67)	<u>4.4.4.4.4.</u> 4.4.4.4.2.	<u>4.4.1.0.0.</u> 4.1.0.0.0.	31 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
147 (p. 22)	<u>0.0.0.0.0.</u> 4.4.1.0.0.	<u>0.0.0.0.0.</u> 0.0.0.0.0.	30 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
170	<u>4.4.4.4.4.</u> 4.4.0.0.0.	<u>4.4.4.0.0.</u> 0.0.0.0.0.	39 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
244	<u>4.4.4.3.0.</u> 4.4.4.0.0.	<u>4.4.1.0.0.</u> 0.0.0.0.0.	25 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
262 (p. 62)	<u>4.4.4.4.4.</u> 4.4.4.4.0.	<u>4.4.4.0.0.</u> 0.0.0.0.0.	17 "	3 doses of 0.9 grm. of neosalvarsan intravenously.
309 (p. 32)	<u>4. - - - -</u> 4.4.4.0.0.	<u>0.0.0.0.0.</u> 2.0.0.0.0.	13 "	2 doses of 0.9 grm. of neosalvarsan intravenously and 8 injections of mercury cream into the buttock.

* He had previously received 36 inunctions with mercurial ointment.

In the majority of cases the length of time between the two examinations is of little value except as indicating that the reaction became negative in the cerebrospinal fluid within a given number of weeks; we have no evidence that it had not become negative before the date of the second examination given on Table C. But on the whole we can say that the cerebrospinal fluid, though at first strongly positive, usually becomes negative in about six months; within a year all but one of the cases on Table C were completely negative in the cerebrospinal fluid.

The coincident amount of improvement shown by the patient depends entirely on the extent to which his signs and symptoms are, or are not, due to secondary changes in the central nervous system. If hæmorrhage has occurred into the spinal cord, as a consequence of rupture of a vessel weakened by endarteritis syphilitica, the patient will not show improvement coincident with the change for the better in his cerebrospinal fluid. Similarly, if some vascular blocking or local anæmia has led to secondary degeneration in one or more nerve-tracts it is obvious that the consequences of this degeneration will remain and the patient will continue, as before, to be spastic or ataxic. Thus it is of urgent importance to treat the patient early; for meningo-vascular syphilis is singularly amenable to treatment, and the permanent ill-effects due to this form of the disease are mainly due to secondary changes.

CHAPTER V.—SYPHILIS CENTRALIS.

Fournier's conception of "parasyphilis" was a disease which had syphilis for a necessary antecedent, though not in itself a manifestation of the specific virus; he based this view on the insusceptibility of such patients to anti-syphilitic treatment.

Now that we no longer agree with the first part of Fournier's definition but look upon all "parasyphilitic" manifestations as directly due to the activity of the *Spirochæta pallida*, we are obliged to ask ourselves why are diseases such as dementia paralytica and tabes dorsalis so little amenable to anti-syphilitic treatment? For, on the whole, cerebrospinal syphilis responds in a remarkable manner to mercury or salvarsan.

The answer has been given by Fildes and McIntosh [3], who showed that, as usually administered, the arsenical compounds, such as salvarsan and neosalvarsan, do not enter the structure of the central

nervous system in any effective quantity. Hence if the focus of disease lies in the substance of the central nervous system its activity will not be checked by drugs circulating in the blood-stream.

Fournier depended for his generalization on the fact that symptoms and signs in "parasyphilis" were but little influenced by treatment; we can add evidence in the same direction gathered from the behaviour of the Wassermann reaction in the cerebrospinal fluid. For in cases of meningo-vascular syphilis the reaction in the cerebrospinal fluid, if positive, can rapidly be rendered negative by treatment, whilst in "parasyphilis" it is little, if at all, affected.

But apart from this difficulty in reaching the focus of disease by means of such drugs there is another reason why many patients with tabes dorsalis and allied conditions do not respond to treatment. We believe that the neuroglia and essential tissues of the central nervous system have become hypersensitive in consequence of the previous activity of the *Spirochæta pallida*. Tracts of fibres, groups of cells and the neuroglia supporting them have been so highly sensitized that they now react with greater vehemence and to a smaller dose of the virus. Consequently tracts and nuclei degenerate whilst the neuroglia proliferates, and destruction of the nervous system may greatly exceed in extent the actual focus of fresh infective activity. In a case of tabes dorsalis destruction may run to an end in one or more tracts or nuclei and leave the patient in a quiescent stage of the disease with all the signs of gross degenerative changes in the central nervous system. Thus optic atrophy, when it once begins, invariably ends in blindness, but the disease may then make no further advance for many years; in the same way a man may be left with a grave ataxia which does not increase, for the disease has become completely quiescent, at any rate for a time.

Not only does the disease cease to advance but the Wassermann reaction in the cerebrospinal fluid may become negative and even a provocative injection of neosalvarsan may be unable to render it positive. In such patients the excess of cells, associated with the acute stage, may also disappear and the cerebrospinal fluid may not differ from that of a normal person (No. 83, p. 102).

From the clinical aspect however these patients are none the less suffering from tabes dorsalis, for they may show all the classical signs of absent knee-jerks, Argyll-Robertson pupils and gross ataxy; and yet in this quiescent stage there is no disease to treat. The flame has burnt itself out and left dead ashes on its path. In every

case of syphilis centralis it is important to consider how far the conditions presented by the patient are due to progressive disease, or to what extent they are the consequence of the activity of a virus which has ceased, at any rate for a time, to cause destruction in that particular part of the central nervous system.

[A] CLINICAL VARIETIES.

§ 1.—*Dementia Paralytica.*

Much of the confusion which has arisen with regard to the susceptibility of this disease to treatment and the behaviour of the Wassermann reaction in the cerebrospinal fluid springs from the notorious difficulty in making a differential diagnosis by clinical examination alone. There is not a symptom or a sign in dementia paralytica which cannot be present in a case of subacute meningo-vascular syphilis.

But the effect of treatment with anti-syphilitic remedies, especially the arsenical compounds, differs so greatly in the two conditions that the prognosis is fundamentally different. It is consequently impossible to class them together clinically, although in many cases they are indistinguishable at the bedside on the first examination. But by long continued observation and by watching the effect of treatment, not only on the patient but also on the Wassermann reaction in the cerebrospinal fluid, it is possible in many cases to separate these two conditions of such different prognostic import.

Compare the two following cases with one another :—

A woman of 39 (Case 120) was admitted to the London Hospital on June 28, 1912. She was walking along the road when she met a drunken woman whom she did not like ; she became angry and excited and lost her speech. She was unable to move and was taken home in a cart. Next day, when admitted to the hospital, her memory was bad, her speech slurred and thick, but she was not aphasic or apraxic.

There was much tremor and unsteadiness of the left hand when the arm was extended ; the right upper extremity was distinctly paretic and there was some diminution of power in the right lower limb ; the left leg seemed to be unaffected. Both knee-jerks were brisk, but both plantar reflexes gave a flexor response and there was no ankle-clonus. The abdominal reflexes were obtained. The pupils were irregular, at times oval vertically, at times horizontally ; they reacted to light, but the reaction was not maintained and they

fell into obvious oscillation. The reaction to accommodation was good. There was no ptosis, ocular paralysis, nystagmus or other abnormality within the territory of the cranial nerves except that the face was flattened, especially on the right side. The fundi were normal, and the sphincters were unaffected.

Mentally she was dull, confused, worried. She thought "all was wrong at home," had other vague delusions, and could not sleep.

The Wassermann reaction was $\frac{\text{serum } 4.2.0.0.0.}{\text{cs.f. } 4.3.2.0.0.}$ and everything seemed to point to the diagnosis of dementia paralytica. But she was given injections of salvarsan and potassium iodide in considerable doses and an extraordinary change for the better rapidly occurred. By March, 1913, memory, attention and general intelligence had greatly improved and speech was no longer affected. Moreover the Wassermann reaction had become completely negative $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$. This improvement has been maintained; in May, 1914, she no longer showed any nervous manifestations and had returned to her occupation. The Wassermann reaction was still negative in both serum and cerebrospinal fluid.

Here was a case which during the first period of clinical observation could not have been distinguished from one of dementia paralytica. Had she been sent to an Asylum there is little doubt she would have steadily degenerated and have been classed as an obvious instance of "general paralysis." After death no close microscopical examination would have been made in so commonplace a case and she would have swelled the list of those dying from that disease.

A Case indistinguishable from one of "General Paralysis" where, under Treatment, both the Patient Recovered and the Wassermann Reaction became Negative in the Cerebrospinal Fluid.

Case 120.—A. P., female, married; born 1874. In 1893, at the age of 19, she married her first husband, who died of "drink" four years later; to him she bore two children, one born in 1894, who died as a baby of "bronchitis," and a second born in 1896, who survived and is healthy. Shortly after marriage she suffered from a series of bad throats and her hair fell out.

In 1898 she married her second husband, and by him she has had (1) a child born in 1899 who died of "wasting," (2) a girl born in 1901, (3) a girl born in 1903, (4) a girl born in 1906, (5) a girl born in 1908; these pregnancies were followed by three miscarriages. The children born in 1901 and in 1903 give a positive Wassermann reaction in the blood, the child born in 1906 a negative reaction. The second husband also gives a positive reaction in the serum.

Four weeks before her admission on June 28, 1912, this patient miscarried. After the miscarriage she "never seemed well," and on June 27, 1912, she had a seizure, followed by loss of speech and paresis of the right hand.

On admission on June 28, 1912, she was muddled, inattentive and worried. She complained repeatedly that "everything was wrong at home," when in fact this was not the case. She was subject to causeless attacks of crying. Her memory was very defective. She only spoke when addressed, but her answers to questions were logical and to the point. Her speech was dysarthric, syllables were frequently slurred and badly pronounced. She did not complain of headache and was not subject to attacks of vomiting. Vision was unaffected. The vessels of the fundi were tortuous, but the edges of the optic discs were sharply defined. Hearing, smell and taste were unaffected.

The left eyelid drooped slightly but ocular movements were well carried out. The pupils were unequal in size, irregular in outline and only reacted sluggishly to light with the development of hippus; they reacted well to accommodation. Both sides of the face were flattened and there was definite paresis of the upper and lower halves on the right side. The tongue was very tremulous and on protrusion deviated to the right. The movements of the palate and larynx were unaffected.

Both hands were extremely tremulous. The right arm was paretic and the grasp of the right hand was feeble. The alignment of the fingers of the left hand was bad. No difference could be discovered between the muscular tone of the two upper extremities. There was some paresis of the right lower limb which cleared up rapidly after admission.

As far as could be determined there was no sensory loss.

The knee-jerks were clonic, the ankle-jerks were extremely brisk, but ankle-clonus could not be obtained. The wrist- and elbow-jerks were exaggerated. The abdominal reflexes on both sides were obtained. On the right side the plantar reflex gave a doubtfully extensor response, whilst on the left it was definitely flexor.

The sphincters and the movements of the spine were completely unaffected.

The urine contained albumen, and some granular casts were present. The vessels were thickened and tortuous and the left ventricle was enlarged. The blood-pressure in the brachial artery was 215 mm. The lungs were emphysematous. No abnormal physical signs were discovered in the abdomen.

On July 3, 1912, the Wassermann reaction was $\frac{\text{serum } 4.2.0.0.0.}{\text{cs.f. } 4.3.2.0.0.}$

She was given 0.6 gm. of salvarsan on July 6, 1912.

Eight months later, on March 5, 1913, the reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered less than 1 per cubic millimetre.

On March 7, 1913, she was given 0.9 gm. of neosalvarsan.

Since this treatment the serum has been tested on June 25, 1913, and on November 22, 1913, and on both occasions reacted negatively. On April 30, 1914, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells again numbered less than 1 per cubic millimetre.

In May, 1914, both pupils reacted to light, though somewhat sluggishly and with a tendency to hippus. The face was still a little flattened on the right side, but there were no other abnormal signs in the territory of the cranial nerves. The reflexes were as before, but motion had greatly improved and no difference in power could be discovered between the two hands. She could now cut out dresses and fulfil all her domestic duties.

The brachial blood-pressure still measured about 200 mm. and albumen was still present in the urine.

Compare the case of this woman with the following characteristic instance of dementia paralytica (No. 32). At first sight the likeness between the two is astonishing, but they differed in the consequences of treatment and the behaviour of the Wassermann reaction in the cerebrospinal fluid.

The patient was a man of 40, who, for about sixteen months before admission to the London Hospital, had complained of double vision and failure of sight in the right eye. He had been troubled for some time with shooting pains in the right leg, and, later on, in the right half of the trunk, associated more recently with weakness of the right arm and leg.

He was unusually well educated and intellectual, but his memory had become defective and he had lost the power of concentrating on his work. He was irrational, his attention was easily diverted, and he had lost his business instinct.

Speech was slurred, with indistinct articulation and a tendency to miss out syllables. The right hand was weak and tremulous and power was diminished in the right leg. There seemed to be some inco-ordination of the right upper extremity. His knee-jerks could be obtained but the ankle-jerks were abolished. Both the plantar and the abdominal reflexes responded normally. The right pupil was irregular in shape and larger than the left; both reacted badly to light, but readily to accommodation. The right external rectus and inferior oblique were weak, and diplopia was present when he moved his eyes to the right. The face was expressionless and flattened and the tongue was tremulous.

The Wassermann reaction was $\frac{\text{serum 4.4.4.2.1.}}{\text{cs.f. 4.4.4.3.2.}}$

He received two doses of 0.6 grm. of salvarsan, but grew steadily worse, and fourteen months later was an even more obvious case of dementia. He was loquacious and did not finish his sentences. He could not answer even simple questions because his attention wandered. He seemed to have no recollection of anything that had

happened during his last stay in the Hospital, and his memory was extremely bad.

His speech was profoundly slurred, and syllables and whole words were missed out. Gait was very unsteady and the movements of the upper extremities clumsy and inco-ordinate. There was no paralysis and the difference between the extremities on the two sides had disappeared. Both knee-jerks were obtained with difficulty; the right plantar reflex was usually extensor, whilst the left gave a flexor response. The pupils still reacted sluggishly to light, but the right was larger than the left and both were in shape irregularly oval. Lips and tongue were extremely tremulous. The sphincters were now affected and he suffered from overflow incontinence of urine.

The Wassermann reaction was $\frac{\text{serum 4.4.4.4.0.}}{\text{cs.f. 4.4.4.2.0.}}$ almost identical with that obtained fourteen months before. Further injections of neo-salvarsan failed to check his downward course.

A Case of Dementia Paralytica where the Positive Wassermann Reaction in the Cerebrospinal Fluid remained almost unaltered Fourteen months after Treatment.

Case 32.—J. C., male, married, tailor; born 1872. In 1893, at the age of 21, when serving in the Russian Army, this patient caught "gonorrhœa" and suffered from a "running" which was not followed by any rash, sore throat, or other manifestation of secondary syphilis. He was treated for a few weeks only, and until the time of his marriage enjoyed good health.

In March, 1910, he married; his wife had never been pregnant. Shortly after his marriage he began to suffer from attacks of shooting pains in the legs, and later from "curious sensations" in his head and double vision, accompanied by a failure of the sight of the right eye. In the course of the next year his memory became defective; he lost all sexual power and began to complain of a weakness of the right half of his body. At that time he became less capable in business, his writing lost character and he became grandiose in his ideas.

He first came under observation in June, 1912, when he was admitted to the London Hospital under the care of Dr. Robert Hutchison.

He was a well-educated Hebrew, who had spoken four languages. He was intelligent but irrational. He had lost all business instinct. He talked freely of grand schemes by which he was going to change the face of Nature and make untold sums of money. During conversation the magnitude of these ideas could be raised by increasing degrees. His memory for recent events was extremely bad. He complained immediately after a big meal that "he was being starved," and said that "he was totally unable to sleep and had not slept a wink" after a good night's rest. His attention was fleeting. He

had not suffered from seizures or attacks of vomiting. His speech was slurred and many syllables or words in a sentence were missed out; this defect in speech was equally noticeable in Yiddish and in English.

He complained of headache over the right frontal region, but the scalp was not tender on pressure. Hearing, smell, taste, and vision were unaffected and the optic discs and fundi were normal.

He complained of double vision whenever he looked far to the right. The right external rectus and right inferior oblique muscles were paretic; but on closure of the left eye the right eyeball was seen to move freely in all directions. The right pupil was wide and eccentric and its margins were irregular; the left was well centred and regular in outline; both reacted sluggishly to light and briskly to accommodation. The face was flattened and tremulous in movement. The tongue on protrusion came out straight and was held steadily. The movements of the jaws, palate, and larynx were normal.

His gait was unsteady, but Romberg's sign was not obtained. The right hand could not be used to carry out fine movements and the tremor was visible in his writing. The writing was illegible and often undecipherable because words and syllables were missed out. The grasp of the right hand was feeble. The power of the right leg was weaker than that of the left.

His answers to the tuning-fork, the compasses, the prick of a pin, and the hot and cold tubes and to the tests for recognition of posture and passive movement were more accurate and more ready on the left half of the body than on the right; but there was no complete loss of sensibility anywhere. The answers obtained when using cotton-wool as a stimulus were more accurate than those obtained with any other form of testing.

On the left side the knee-jerk was brisk but the right was obtained on reinforcement only. Ankle-jerks could not be obtained. The abdominal reflexes were brisk. On the left side wrist- and elbow-jerks were readily obtained, on the right side they were doubtful. Both plantar reflexes gave a flexor response.

The patient had experienced no difficulty in holding or passing water, and no gross signs of disease were discovered in the heart, vessels, lungs, abdomen or urine.

On June 5, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.1.}{\text{cs.f. } 4.4.4.3.2.}$

On June 7, 1912, he was injected with 0.6 gm. of salvarsan and this dose was repeated on June 12. On June 18, 1912, without a word of explanation he walked out of the hospital, went to a shop and ordered four suits of dress clothes and half a dozen top-hats.

He was not seen again until August 15, 1913, when he had altered but little mentally. He was loquacious and started many sentences, but rarely finished any statement. His answers to simple questions were irrational and inconsequent; his wife volunteered the statement that in Yiddish his answers were also bad. He could not remember any details of his previous admission to Hospital and denied that he had ever been an in-patient anywhere before.

Between June, 1912, and August, 1913, he had suffered from no seizures or attacks of vomiting. His speech was not much worse than on the previous admission. Vision was good and the optic discs and fundi appeared normal. The eye-movements were still defective, the face was flattened and the lips and tongue extremely tremulous. The movements of the hands were clumsy and the head and trunk took part in every volitional movement of the hands.

Both knee-jerks were sluggish, but could be elicited on reinforcement. The ankle-jerks were absent. The plantar reflexes either gave no responses or a sluggish extension. The jaw-jerk was much exaggerated.

Occasionally he wetted himself by day, and by night passed his water into the bed. Since his previous admission he had not been able to produce an erection.

On August 20, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 4.4.4.2.0.}$ and the cells numbered 24 per cubic millimetre.

The majority of patients with dementia paralytica, seen in the practice of a General Hospital in this country, approximate more to the type of tabo-paresis. The dementia usually causes loss of memory and aptitude for work with no exaltation or delusions; for any patient with acute mental symptoms finds his way rapidly into an Asylum by way of the Workhouse Infirmary, and does not pass through the hands of the neurologist.

Thus the cases of dementia paralytica used in this research are not a fair sample of the population, but are biassed in one direction in consequence of that complete divorce between neurology and psychiatry which unhappily obtains in this country. Although many of our patients ultimately entered an Asylum, they came to the Hospital not for mental symptoms but for seizures, loss of memory, or inability to work. They usually showed some affection of speech, tremor of the hands, face, and tongue, Argyll-Robertson pupils, and not infrequently absent knee-jerks with or without ataxy.

The following case (No. 200) is a good example of this condition. He was a man of 29, who was sent to us from the Rockefeller Institute, New York, for intensive treatment. At first the signs were those of tabes dorsalis, associated with tremor of the face and tongue and obvious mental instability. His general intelligence was not, however, greatly diminished. The Wassermann reaction was completely positive in the cerebrospinal fluid, and has remained so up to the present time in spite of intensive treatment with neosalvarsan intravenously and with serum injected into the lumbar sac after the method of Swift and Ellis [21]. At the same time his symptoms have become much

aggravated, and he is now grandiose and exalted; his speech is profoundly affected, and the tremors have greatly increased.

A Case of Tabo-paresis with a completely Positive Wassermann Reaction in the Cerebrospinal Fluid; this remained Unaltered in Strength in spite of much Treatment and the Patient grew steadily worse.

Case 200.—S. D., male, single, accountant; born 1883. This patient contracted syphilis in 1900, at the age of 17; he suffered from a chancre only and was treated with mercury and iodides by the mouth for eighteen months; no secondary manifestations of syphilis followed.

In the summer of 1911, he lost sexual desire, due, as he thought, to abuse of alcohol. In January, 1912, his left foot "became dead," and he then found that he could no longer hurry or jump and that he was unsteady when walking in the dark. About December, 1912, he began to suffer from pains in the legs, and for these he attended Dr. Arthur Ellis, of the Rockefeller Institute, New York, who sent him to us for "intensive treatment with salvarsan."

He first came under our observation in May, 1913, and was admitted to the London Hospital on June 8, 1913.

At this time he was irrational, emotional and subject to attacks of crying. Memory and attention were fair and his speech little affected. He could reason, but doubted his own conclusions. He had never suffered from headache or attacks of nausea or vomiting.

Vision was unimpaired, the optic discs were healthy, and hearing, smell, and taste unaffected.

The right pupil was larger than the left; both responded sluggishly to light and the contraction was ill-sustained, but they reacted briskly to accommodation. The movements of the eyes, face, palate, and larynx were normal, but the tongue, though protruded straight, could not be held steadily and was intensely tremulous.

His gait was ataxic and Romberg's sign was present. The alignment of his fingers was bad, and on closing the eyes the outstretched hands fell away from the position in which he intended to hold them. The muscles of the extremities were well developed and showed no loss of tone.

He complained of shooting pains in the legs and of a constant "gnawing ache in his knees." In the lower extremities there was much loss of the power of appreciating posture and passive movement, the compasses and the vibrations of the tuning-fork. He recognized the shape, size, form and consistence of objects placed in his hands with difficulty. To tests with cotton-wool, with the prick of a pin and with the hot and cold tubes no disturbance of sensibility could be discovered.

Neither knee-jerk could be obtained even on reinforcement, and the ankle-jerks were abolished. The wrist- and elbow-jerks were normal and the abdominal reflexes brisk, but no plantar reflexes could be obtained on stimulation either of the soles or of the front of the ankles.

He experienced no difficulty either in holding or in passing water, but for two years he had been unable to produce an erection of the penis.

No abnormal signs were discovered in the heart, lungs, or abdomen, and the urine contained neither albumen nor sugar.

On June 11, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.3.}}{\text{cs.f. 4.4.4.4.4.}}$ and the cells numbered 22 per cubic millimetre.

He was injected intravenously with doses of 0.9 gm. of neosalvarsan on June 12 and June 21, 1913; after each injection he complained of much headache, nausea, and vomiting, and on June 22 his temperature rose to 101° F. (38.3° C.). The attack of vomiting after the first injection lasted sixty hours and during this time morphia only, of the many drugs administered, had any effect either in quieting the patient or in stopping the attack of vomiting. On June 23 he developed a temporary state of mental confusion in which he constantly repeated commands and statements such as "thanks very much," and laughed immoderately; yet when his attention was gained his conversation was rational and his ideas consecutive. This attack lasted some twenty-four hours and during this time he vomited six times. On June 27 he seemed to have returned to the state in which he was admitted; 0.9 gm. of neosalvarsan were administered; no abnormal reaction followed this injection.

After this he was discharged and treated with potassium iodide from July 1 until September 29. He was then injected intravenously on:—

September 29 with 0.2 gm. of neosalvarsan.

October 3 " 0.3 " " "

October 7 " 0.3 " " "

October 10 " 0.3 " " "

On January 14, 1914, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.4.}}{\text{cs.f. 4.4.4.4.4.}}$ and the cells numbered 3 per cubic millimetre.

In January, 1914, his mental condition was worse than it had been in the previous June. He was self-conscious, restless, excitable, and exalted, boasting freely of his great abilities. He was intelligent, argumentative and self-opinionated, but at the same time obsequious and deferential. He said that he could walk miles and was the equal of any man living in fighting, although his gait was ataxic and his power of walking poor. He talked freely to sister and nurse about sexual matters. His memory was very defective and his power of attention poor. Sleep was disturbed but was not accompanied by dreams or nightmares.

His speech was extremely jerky and his words badly enunciated, whilst his writing was tremulous, unsteady, and hardly decipherable.

His lips and tongue were intensely tremulous and in every minor action of his hands his whole body moved. Otherwise no fresh manifestations could be discovered within the territory of the cranial nerves.

He stood stiffly at attention and walked with a stamping, ataxic gait, waiving his arms and swaggering with exaltation at his prowess. The left leg was more ataxic than the right, and the upper extremities clumsy and incoordinate.

He no longer complained of pains and on this account was intensely pleased,

and talked to everybody he met about the wonderful improvement he had made under the new therapeutic method. With these exceptions his physical signs were unchanged.

On January 16, 1914, he was again injected with 0.9 gm. of neosalvarsan, and on January 22, February 10, 17, and 22, he was given intrathecally doses of 10 c.c. of his own "salvarsanized serum," collected sixty minutes after the injection of January 16.

Since this treatment no improvement, either in mental or physical state, has occurred, and he is now (July, 1914) a characteristic example of tabo-paresis with exaltation and delusions of grandeur.

On July 8, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.4.}$ and the cells numbered 18 per cubic millimetre.

We have collected in the course of this research 22 cases of dementia paralytica and tabo-paresis, including three instances of the juvenile form of the disease. In every case, as will be seen from Table D, the cerebrospinal fluid gave a strong positive reaction. Our results, as far as they go, agree exactly with the original statement of Plaut and with Mott's observations on Asylum patients with dementia paralytica. The more carefully patients are differentiated by clinical observation and by watching the results of treatment on the cerebrospinal fluid, the greater will be the percentage of positive reactions obtained in cases of dementia paralytica; we have not yet seen an instance of a negative Wassermann reaction in the cerebrospinal fluid.

Thus, in conclusion, we believe that cases of syphilis meningo-vascularis cerebri may be distinguishable from dementia paralytica solely by the fact that the cerebrospinal fluid, from the first, gives a negative reaction. But if, as is so commonly the case, some intraspinal complication is present, the cerebrospinal fluid in both diseases may be equally positive; they are then not infrequently indistinguishable from one another, except by watching the effect of treatment. For in dementia paralytica the symptoms and signs do not improve to any considerable extent, and the positive Wassermann reaction is not materially reduced in the cerebrospinal fluid, even by the most energetic treatment with salvarsan and neosalvarsan.

This we attribute to the situation of the lesions in syphilis centralis, of which dementia paralytica is the cerebral form; the focus of infection lies deep in the nervous system in parts not in direct connexion with the blood-stream. Consequently drugs circulating in the blood cannot materially affect the lesion in central syphilis of the nervous system.

TABLE D.—THE INCIDENCE OF THE WASSERMANN REACTION IN DEMENTIA PARALYTICA AND TABO-PARESIS.

No. of case	Result on first examination	No. of case	Result on first examination
20 (Autopsy)	serum 4.4.4.3.1. cs.f. 4.4.4.4.1.	119 (Autopsy)	serum 4.4.4.4.4. cs.f. 4.4.4.4.4.
32 (p. 92)	4.4.4.2.1. 4.4.4.3.2.	152	4.4.4.3.1. 4.4.4.0.0.
33	4.4.4.4.4. 4.4.4.0.0.	165	4.4.3.2.1. 4.4.4.4.0.
80	4.4.4.3.2. 4.4.4.4.4.	169	4.4.4.4.4. 4.4.4.4.4.
82	4.4.3.1.0. 4.4.4.4.1.	200 (p. 95)	4.4.4.4.3. 4.4.4.4.4.
84 (Autopsy)	4.4.4.4.4. 4.4.4.4.4.	214	4.4.4.4.1. 4.4.4.4.4.
90 (Autopsy)	4.4.4.4.2. 4.4.4.4.0.	230 (Autopsy)	4.4.4.4.4. 4.4.4.4.4.
95	4.4.4.3.2. 4.4.4.3.2.	285	4.4.4.4.2. 4.4.4.4.2.
96 (Autopsy)	4.4.4.4.3. 4.4.4.4.2.	304	4.4.4.4.4. 4.4.4.4.0.
108	4.4.4.4.0. 4.4.4.4.3.		

JUVENILE.

No. of case	Result on first examination	No. of case	Result on first examination
16 (Autopsy)	serum 4.4.4.4.4. cs.f. 4.4.4.4.4.	197	serum 4.4.4.4.4. cs.f. 4.4.4.2.0.
109	4.4.4.4.4. 4.4.4.4.3.		

§ 2.—*Tabes Dorsalis*.

Year by year the line, once so firmly drawn between tabes dorsalis and dementia paralytica, grew fainter as the identity of the pathological process underlying the two diseases was recognized. Cases were described which started as tabes dorsalis and ended in dementia paralytica, and destruction of the posterior columns of the spinal cord was often found *post mortem* in characteristic instances of "general

paralysis." With the invention of "taboparesis" as a diagnostic expression, the boundaries between the two diseases fell once for all; it was recognized that they were not two separate pathological states, but manifestations of the same process attacking different parts of the central nervous system.

In the same way the conception of *tabes dorsalis* had to be widened to take in atrophy of the muscles and occasionally even lateral sclerosis; primary optic atrophy, associated with normal reflexes, has also been included amongst the forms of *tabes dorsalis*. (Nonne [13], p. 174.) Here also no natural boundaries can be erected between these various "parasyphilitic" states; all of them are manifestations of the same pathological process working on different parts of the nervous system.

All attempts to maintain *tabes dorsalis* as a separate disease must, therefore, be given up and the term confined to a set of signs and symptoms depending mainly on degeneration of the posterior columns of the spinal cord consequent on syphilitic infection. Thus the word *taboparesis* may be used to describe a case with definite signs of affection of the posterior columns of the cord which at the same time or subsequently showed loss of memory, seizures, altered speech, or paresis, pointing to a corresponding form of cerebral affection. In the same way it is better to speak of amyotrophy and *tabes dorsalis*, rather than of "amyotrophic *tabes*"; for the two conditions are caused by the same process acting on different structures, and neither is in the strict sense of the word a disease.

In this section we shall deal solely with cases in which the principal signs pointed to affections of the posterior columns of the spinal cord. "Taboparesis" has been included with *dementia paralytica*; amyotrophy, primary optic atrophy, and epilepsy, due to syphilis *centralis*, will be dealt with in subsequent sections.

The signs upon which we shall depend to show the affection of the posterior columns are absence of the ankle-jerks and knee-jerks accompanied by certain changes in sensation with or without some ataxy of the upper or lower extremities. These changes in sensation consist for the most part in diminished appreciation of the vibrations of a tuning-fork ($C. = 128$), inability to recognize the position into which the segments of the limb have been placed passively, and failure to appreciate the compass-test even when the points are separated to extreme distances, such as 15 cm.

Such then are the signs upon which we have relied in constructing the following table. All cases of *taboparesis* have been included under

dementia paralytica, and the other varieties of syphilis centralis ("para-syphilis") have been relegated to their appropriate sections. For tabes dorsalis can no longer be looked upon as a disease, but is one variety only of central syphilis of the spinal cord.

TABLE E.—THE INCIDENCE OF THE WASSERMANN REACTION IN TABES DORSALIS.

No. of case	Result on first examination	No. of case	Result on first examination
14	serum 4.4.4.4.4. cs.f. 4.4. - - -	132	serum 4.4.0.0.0. cs.f. 4.4.4.0.0.
23	4.4.4.4.4. 4.3.0.0.0.	142	4.4.4.0.0. 4.4.4.0.0.
27	4.4.4.3.0. 3.1.0.0.0.	143	4.4.4.4.0. 4.4.1.0.0.
30	4.1.0.0.0. 4.4.4.4.0.	144 (p. 104)	0.0.0.0.0. 0.0.0.0.0.
37 (p. 107)	4.4.2.0.0. 4.4.3.1.0.	145	4.3.2.0.0. 4.4.3.3.0.
46	4.4.4.4.3. 3.0.0.0.0.	150	4.4.4.4.2. 4.4.3.0.0.
50	4.4.4.4.1. 0.0.0.0.0.	199 (p. 118)	4.4.4.4.0. 4.4.4.4.0.
55	4.3.1.0.0. 4.4.3.1.0.	224 (p. 119)	4.4.4.4.4. 4.4.4.0.0.
56	4.4.4.4.1. 4.4.4.4.1.	234	4.4.4.4.4. 4.4.3.1.0.
58	4.3.1.0.0. 4.4.4.1.0.	257	4.4.4.4.0. 4.4.0.0.0.
67	4.3.2.0.0. 4.4.4.0.0.	258	4.4.4.4.0. 4.4.4.0.0.
70	4.4.4.2.0. 4.3.0.0.0.	278	4.4.4.0.0. 4.4.4.0.0.
83 (p. 102)	2.0.0.0.0. 0.0.0.0.0.	294	4.4.4.4.0. 4.4.4.4.0.
112	4.4.4.4.4. 4.4.4.4.4.	295	4.4.4.4.0. 4.4.2.0.0.
117	2.0.0.0.0. 4.4.4.4.1.	300	4.4.4.4.4. 4.4.4.4.0.
131*	4.3.2.1.0. 4.4.4.3.1.		

* An account of this case was given in BRAIN, 1913, vol. xxxvi, p. 12.

With regard to the Wassermann reaction in *tabes dorsalis*, we have little to say that is not in complete agreement with the statements of other observers. Out of thirty-one cases twenty-eight were positive in cerebrospinal fluid, a result in general harmony with that of Nonne and Mott.

Two of the cases (No. 83 and No. 144) which gave a negative reaction in the cerebrospinal fluid are extremely instructive.

No. 83 was a man aged 55, who was infected at the age of 27. Some five or six years later he began to suffer from shooting pains in his legs, and slowly became ataxic. At the age of 42 he was an outpatient at the London Hospital with obvious *tabes dorsalis*, but for many years before this he had suffered from occasional retention of urine.

In April 1913, at the time our first observations were made, he was admitted because he had suddenly developed a Charcot knee.

He was profoundly ataxic, and fell when his eyes were closed; the muscles of legs and thighs were grossly hypotonic. All power of recognizing vibration, posture, and passive movement was lost in both lower extremities, and there was much delay, though no absolute loss, in the appreciation of pain, heat, and cold. Knee- and ankle-jerks were abolished. Neither pupil responded to light, and the right external rectus acted feebly. The left knee was disorganized, and much distended with fluid. Retention of urine with overflow was present, the bladder reaching to the umbilicus on admission.

Here was a straightforward case of *tabes dorsalis*, but the Wassermann reaction was $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells in the cerebrospinal fluid were not in excess of normal. He was given two injections of 0.9 gm. of neosalvarsan, but no provocative reaction was produced. Evidently we were dealing with a case where the disease had died out, leaving behind it destruction of the posterior columns of the spinal cord.

Compare with this patient No. 144, who also yielded a negative reaction in the cerebrospinal fluid. He was a man aged 42, who was infected with syphilis at the age of 30; this was followed by a chancre and rash, but he was treated for one month only.

In April, 1908, he began to notice numbness of the legs with pains and dribbling of urine. He was then treated with mercury by the mouth, and probably with injections of salvarsan in Canada.

When admitted to the London Hospital in July, 1912, he was

intensely ataxic, and could not stand at all. All the muscles of the lower extremities, and to a less extent those of the arms, were hypotonic. Vibration was not appreciated anywhere below the level of the nipples, and recognition of posture and passive movement was lost in the legs, and gravely diminished in the arms. Sensation of pain, heat, and cold was delayed below the level of the groins, but was not completely lost. The knee-jerks and ankle-jerks were abolished and the wrist-jerks were obtained with difficulty. He suffered from true incontinence of urine, and at times had attacks of rectal tenesmus.

His Wassermann reaction was negative in the serum and cerebrospinal fluid. On July 18 he was given 0.6 gm. of neosalvarsan, and on July 24 and 25 the reaction was $\frac{\text{serum } 1.1.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$; on July 29 and 30 it was $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f. } 0.0.0.0.0.}$. The next day (August 1) he was given another injection of 0.9 gm. of neosalvarsan; and on August 7 the reaction was $\frac{\text{serum } 4.4.4.3.1.}{\text{cs.f. } 1.0.0.0.0.}$. By October 8 it had again become completely negative, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and so it remained.

Here, then, is an instance where the disease was not active, but had not entirely burnt itself out; an injection of neosalvarsan could provoke a positive reaction in the serum, though not in the cerebrospinal fluid, which remained negative throughout, showing that in the central nervous system the activity of the pathological process was apparently at an end.

A Case of Tabes Dorsalis where the Infection had apparently died out. Negative Wassermann Reaction in the Cerebrospinal Fluid.

Case 83.—E. I., male, married, general dealer; born 1858. In 1885, at the age of 27, this patient contracted a chancre, which was followed by the development of a bubo in the right groin. He received treatment for four weeks only.

In 1890 he began to complain of shooting pains in the legs; these were soon followed by the development of ataxy and trouble with micturition.

In 1901 he attended as an out-patient at the London Hospital for incontinence of urine and "cystitis," and was diagnosed as a case of tabes dorsalis on the absence of his knee-jerks, the presence of lightning pains, ataxy and Argyll-Robertson pupils.

In the Autumn of 1912 a large painless swelling of the left knee appeared; in four days the swelling became so great that he was no longer able to walk.

He has attended at the London Hospital since December, 1912, and was admitted in April, 1913, when he showed all the signs of *tabes dorsalis*. His mental state was unaffected, and his speech natural. In the past he had been subject to attacks of vomiting, but not in recent years. The optic discs were pale, but the vessels were of normal size and there were no signs of optic atrophy. Vision, smell, taste and hearing were unaffected.

There was no ptosis. The right external rectus muscle acted weakly, otherwise the ocular movements were normal. The left pupil was larger than the right; both were excentric and neither reacted to light, but they reacted well to accommodation. The features were flattened, but there was no paresis of the face and the tongue on protrusion came out straight and was held steadily.

His gait was characteristically ataxic and Romberg's sign was present. The legs were gravely hypotonic, but the tone of the muscles of the arms was unaffected, and the alignment of the fingers was good.

He complained of occasional spontaneous shooting pains in the legs, which he stated were much less severe than they had been at the onset of the nervous manifestations. To tests on the legs and on the trunk below the level of the umbilicus with the hot and cold tubes, with the prick of a pin and painful pressure there was considerable delay before answers were obtained. He had completely lost all power of appreciating posture and passive movement and the vibrations of the tuning-fork on both legs. The weight, size, shape, form and consistence of objects placed in the hands were well recognized and there was no falling away of the outstretched hands on closure of the eyes. On the legs the light touch of cotton-wool was less affected than any other form of sensibility. To the dragged point of a pin and the pinching of the skin there was definite hyperalgesia over the distribution of the eleventh and twelfth thoracic nerve-roots.

Superficial bed-sores were present on the sacrum. The left knee showed all the characteristics of Charcot's disease, and was enormously swollen; it allowed great lateral displacement and an X-ray photograph showed much bony erosion and change.

The knee-jerks were abolished and the ankle-jerks could not be obtained. The wrist- and elbow-jerks and abdominal reflexes were natural, and both plantar reflexes gave flexor responses.

He had difficulty in passing his urine and on admission was suffering from overflow from a bladder distended to the umbilicus; he had no difficulty in controlling his motions even when soft. The spine was straight and moved naturally.

The cardiac sounds were clear and the lungs emphysematous. The blood-pressure on the right brachial artery was 120 mm. The urine was alkaline and contained much pus and albumen.

On April 9, 1913, the Wassermann reaction was $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

On April 10, 1913, he was injected with 0.9 grm. of neosalvarsan. To this injection no provocation of the Wassermann reaction occurred, for on April 21, 1913, it was still $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

Under rest in bed the swelling of the left knee diminished and on May 30, 1913, he was discharged wearing a long poroplastic splint, feeling "better than he had felt for years."

A Case of Tabes Dorsalis with a Negative Wassermann Reaction in the Serum and Cerebrospinal Fluid. A "Provocative" Positive Reaction appeared in the Serum after Treatment, but not in the Cerebrospinal Fluid.

Case 144.—A. S., male, single, shoemaker; born 1870. In 1900, at the age of 30, he contracted syphilis and suffered from a chancre, which was not followed by any rash or sore throat; he treated himself for four weeks with mercury.

In April, 1908, he began to be troubled with numbness in the legs, and about August of that year first experienced difficulty in walking. Shortly after the development of these symptoms he began to have difficulty in starting the act of micturition, and later suffered from incontinence of urine from overflow. About the same time he began to suffer from attacks of sharp shooting pains in the legs and a sense of fulness in the throat. From April, 1908, until July, 1909, the symptoms increased very rapidly, and in the latter month he was admitted to the Ottawa Hospital, where he received a course of inunctions with mercury. He remained an in-patient until November, 1909, but despite the mercurial treatment new symptoms continued to develop. In February, 1910, he was admitted to the Montreal Hospital and was treated with injections of salvarsan and also of mercury. Under this treatment the active progress of his symptoms subsided, and between July, 1910, and July, 1912, no fresh manifestations appeared.

He was admitted to the London Hospital in July, 1912, and remained an in-patient until December, 1912. His mental state was normal and his speech was unaffected. He was subject to irregular pyrexial attacks, in which the temperature rose to 100° F. (37.7° C.) without apparent cause. In these pyrexial attacks the rate of the pulse increased correspondingly from about 88 to 100 beats per minute. He complained of no headache. During the months of October, November, and December, 1912, he was subject to paroxysmal vomiting (gastric crises) lasting on each occasion one or two days. Whilst an in-patient he also suffered from attacks of rectal tenesmus (rectal crises) and occasional difficulty in swallowing.

Vision was unaffected. The optic discs were pale, the vessels of the fundus small, but there was no definite evidence of primary optic atrophy. Hearing, smell, and taste were unaffected.

The right external rectus muscle was completely paralysed and the patient suffered from a permanent squint. The pupils were small and their outlines were irregular; neither reacted to light, but both reacted to accommodation.

The face was flattened and expressionless. The movements of the tongue, palate, and larynx were unaffected.

The gait was intensely ataxic, and he could not stand at all with his eyes closed. The musculature of the lower extremities was poorly developed and the muscles themselves were hypotonic.

He complained of spontaneous grinding and shooting pains in the legs. There was grave loss of the sense of posture and passive movement in the hips, knees, ankles, toes, and considerable loss in the fingers, wrists, and elbows. Below the level of the nipples on both sides he could not appreciate the vibrations of a tuning-fork. The response to the prick of a pin, to painful pressure, to heat and cold in both legs was impaired and greatly delayed. Everywhere the appreciation of cotton-wool was less affected than any other form of sensibility.

The knee-jerks and ankle-jerks were abolished. The abdominal reflexes were readily obtained and the plantar reflexes on both sides gave brisk flexor responses. The jaw-jerk was natural.

He could not hold his water, and suffered either from incontinence of urine or precipitancy in micturition; he complained of attacks of rectal tenesmus, but at other times experienced no difficulty in controlling his motions.

The spine moved freely, but showed a general dorso-lumbar convexity.

His vessels were thickened and tortuous, but no abnormal signs were discovered in the heart, lungs, abdomen, or urine.

On July 10, 1912, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and on

July 16, 1912 $\frac{\text{serum } -. -. -. -.}{\text{cs.f. } 0.0.0.0.0.}$

On July 18, 1912, he received 0.6 gm. of neosalvarsan and the reaction was tested on

July 18, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -. -. -. -.}$

July 20, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -. -. -. -.}$

July 22, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -. -. -. -.}$

July 24, $\frac{\text{serum } -. -. -. -.}{\text{cs.f. } 0.0.0.0.0.}$

July 25, $\frac{\text{serum } 1.1.0.0.0.}{\text{cs.f. } -. -. -. -.}$

July 29, $\frac{\text{serum } -. -. -. -.}{\text{cs.f. } 0.0.0.0.0.}$

July 30, $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f. } -. -. -. -.}$

It will be seen that a "provocative" reaction appeared in this case in the serum, but not in the cerebrospinal fluid, seven to twelve days after an injection of 0.6 gm. of neosalvarsan.

On August 1, he received another injection of 0.9 gm. of neosalvarsan, and the Wassermann reaction on August 7 was $\frac{\text{serum } 4.4.4.3.1.}{\text{cs.f. } 1.0.0.0.0.}$

On August 10 another injection of 0.9 gm. of neosalvarsan was given, and the reaction on October 8 was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

On October 14 he received another dose of 0.6 gm. of neosalvarsan, and on October 23, 1912, the serum still reacted negatively $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -. -. -. -.}$

Although the serological reactions altered in this manner under treatment no change occurred in the signs or symptoms of disease.

Now although many patients with tabes dorsalis may reach this stage, most of them come under observation at a time when the disease is active and both serum and cerebrospinal fluid are strongly positive. This reaction remains unaltered by anti-syphilitic treatment in tabes dorsalis, as in other forms of syphilis centralis, even although the treatment is carried out over periods amply sufficient to produce a profound change in cases of syphilis meningo-vascularis. But in the course of some years, if the patients survive the various intercurrent complications, a certain proportion tend to pass into a state of quiescence, in which they are left with signs of destruction of some portion of the nervous system, but no active disease. In this stage the Wassermann reaction may become negative in the cerebrospinal fluid.

The majority, however, of the patients with tabes dorsalis come under observation at a time when the disease is actively progressive, and correspond more closely with the following instance.

No. 37 was a man aged 41 who was infected at the age of 25 and treated with mercury off and on for the next ten years. He was admitted to the London Hospital in October, 1912. For many years he had suffered from shooting pains in the legs and in 1904 was discovered to have Argyll-Robertson pupils.

On admission his gait was ataxic and he fell when his eyes were closed. Ataxy was confined to the lower extremities, where there was considerable loss of appreciation of posture, passive movement and vibration. Sensibility to prick was gravely defective, and there was also some want of appreciation of heat and cold. Touch was unaffected. The pupils were irregular and reacted to accommodation but not to light. Knee-jerks and ankle-jerks were abolished. He suffered occasionally from difficulty in passing his water.

His Wassermann reaction on October 8, 1912, was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 4.4.3.1.0.}$

He was given repeated doses of 0.9 grm. of neosalvarsan, but on September 3, 1913, the reaction showed no material change and was
serum 4.4.4.2.0.
cs.f. 4.4.2.0.0.

A Case of Tabes Dorsalis with a Positive Wassermann Reaction in the Cerebro-spinal Fluid. No Material Change under Treatment.

Case 37.—C. C., male, married, cycle agent; born 1871. This patient contracted syphilis in 1896, at the age of 25, and suffered from a chancre, recurrent sore throats, a rash on the chest and aching pains all over. He was treated with mercurial pills by the mouth from 1896 to 1898, and again at intervals during the years 1902 to 1912.

He married in 1891; his wife had one healthy child born in 1896 and no miscarriages.

About 1902 he began to suffer from a syphilitic affection of the tongue, which in the years 1902 to 1908 always yielded promptly to the administration of mercury, until in 1908 it became a typical leucoplakia.

In about 1904 nervous symptoms began with shooting pains in the legs and some degree of ataxia. He is known to have had Argyll-Robertson pupils and an affection of the bladder since 1906; since this time he had always experienced difficulty in obtaining an erection of the penis. Between 1908 and 1912 he believed that the "tabetic" symptoms had been stationary.

In the spring of 1912 an ulcer developed on the right side of his tongue and for this he was admitted on October 4, 1912, to the London Hospital.

On the right half of the tongue was a large epitheliomatous growth, $1\frac{1}{2}$ in. by .1 in. (3.8 by 2.5 cm.), with a shallow ulcer on the outer margin, whilst the rest of the tongue showed a characteristic leucoplakia. No enlarged secondary glands were felt in the neck. The tongue was fairly freely movable, and on October 23, 1912, Mr. Hutchinson removed the right half and the glands of the submaxillary region, and ligatured the right lingual artery in the neck.

His vessels generally were thickened and tortuous; the aortic second sound was accentuated; the lungs showed moderate emphysema, but no abnormal physical signs were discovered in the abdomen or urine.

His mental state and memory were unaffected. Speech was natural, and he had never suffered from attacks of nausea or vomiting. He did not complain of any headache. Hearing, smell, taste and vision were unaffected, and the optic discs and fundi on both sides appeared natural.

Ptosis of the left upper eyelid was present. The left pupil was irregular in outline, oval in shape with the long axis vertical and reacted sluggishly to intense light; the right pupil was well centred and regular in outline but did not react even to the most intense illumination. Both pupils reacted well on accommodation and convergence. The ocular movements were unimpaired. The face moved symmetrically and its expression was normal. The tongue was protruded straight and held steadily. The movements of the palate and larynx were unaffected.

His gait was typically ataxic and Romberg's sign was obtained. There was no muscular wasting. The fingers could be brought into perfect alignment and there was no falling away of the hands on closing the eyes. The tone of the muscles of the legs was almost normal.

He complained of occasional attacks of lightning and grinding pains in the legs. There was considerable loss of the ability to recognize posture and passive movements in the legs, and an almost complete inability to appreciate the vibrations of the tuning-fork and the compass-points on both legs. Painful pressure, the prick of a pin, and the hot and cold tubes were recognized after a delay on both legs, and their recognition led to "drawing away" reflexes of large extent involving the whole of the limb stimulated.

The knee-jerks were completely abolished and ankle-jerks could not be obtained, whilst the plantar reflexes on both sides gave a flexor response. The abdominal reflexes were readily elicited.

The patient complained of precipitancy of micturition and occasional attacks of urinary retention with overflow.

On October 8, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 4.4.3.1.0.}$

He was given 0.9 gm. of neosalvarsan, and before operation the ulcer of the tongue diminished in size. On November 3, 1912, after the operation, he was again injected with 0.9 gm. of neosalvarsan.

On May 4, 1913, he received another injection of 0.9 gm. of neosalvarsan.

On May 7, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f. } 4.4.2.0.0.}$ and the cells numbered 30 per cubic millimetre.

In May, 1913, he stated that since his first injection his general health had much improved, the lightning pains had ceased and were now replaced by bearable discomfort in the legs. At the same time the knee-jerks had reappeared so that the left was now readily obtained and the right could be obtained with reinforcement; the left ankle-jerk was present and the right was brisk. No changes had appeared, however, in the territory of the cranial nerves.

On May 8, 1913, he complained of a tender spot on the inner fold of the right buttock, and here a patch of herpetic vesicles was seen covering an area $\frac{1}{4}$ inch by $\frac{1}{4}$ inch (6 by 6 mm.).

Shortly after this date secondary malignant glands appeared on the right side of the neck. These were treated by further removal and later by X-rays. In July, 1913, the wound broke down and the surface of the skin around the wound ulcerated.

On September 3, 1913, the nervous signs were similar to those found in the previous May, and the Wassermann reaction was identical $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f. } 4.4.2.0.0.}$

In December, 1913, he died of secondary carcinomatosis; and no *post-mortem* examination was allowed.

Thus we believe that, although neither the symptoms nor physical

signs of tabes dorsalis are materially affected by anti-syphilitic treatment the disease in many cases tends to become quiescent. The more nearly this stage is reached the weaker is the Wassermann reaction in the cerebrospinal fluid and the fewer cells does it contain. After a quiescent period, however, the disease may start again; some other structure such as the optic nerves may become affected and run on to complete degeneration.

Thus in tabes dorsalis the character of the Wassermann reaction in the cerebrospinal fluid depends on the state of the disease; if it is actively progressive the reaction will be highly positive and the cells excessive. But if the signs are only the results of a process which has come to an end permanently, or for a time, the reaction may be completely negative in the cerebrospinal fluid, even without anti-syphilitic treatment.

§ 3.—*Muscular Atrophy.*

We have already spoken of those cases of muscular atrophy due to syphilis, where the signs and symptoms are obviously caused by changes in the meninges and vessels. But, as many observers have pointed out, such an explanation does not fit every example of amyotrophy arising on a syphilitic basis, and fails especially in cases where muscular atrophy accompanies tabes dorsalis.

It will be well, therefore, to consider the various views that have been put forward with the hope that we may be able to suggest a solution which will result in greater certainty of diagnosis and prognosis.

In 1893 Raymond [20] brought forward some cases of muscular atrophy in one of which an autopsy was obtained. This revealed vascular and perivascular lesions leading to destruction of the anterior horn-cells. By some curious misapprehension Fournier ([4], p. 262) bases on these cases his view that uncomplicated muscular atrophy may occur in "parasyphilis." Léri [7], however, rightly uses Raymond's observations as a support to his view of the meningo-vascular origin of syphilitic amyotrophy.

Dejerine [1] in 1889 laid stress on the frequent occurrence of muscular atrophy in tabes dorsalis, and attributed it to peripheral neuritis; he was unable to find the degeneration of anterior horn-cells described by Raymond.

Léri [7] in 1903 gathered together six cases of progressive muscular atrophy of syphilitic origin, in two of which an autopsy was obtained. Subsequently with Lerouge [9] he considered the whole question

systematically in the light of seventy-five cases reported in the literature, and came to the conclusion that muscular atrophy of syphilitic origin was due to a diffuse vascular meningomyelitis. He included cases where signs were present of tabes dorsalis, of "general paralysis," or of lateral sclerosis, and explained the slightness of the meningeal changes found after death in such conditions by the gradual subsidence of the acute process. Nonne ([13], p. 418) takes much the same view and does not discuss the relation of these cases to "parasymphilis."

We pointed out [10] that cases of muscular atrophy of syphilitic origin could obviously be divided into two groups. Into the first group fell naturally those where clinical signs pointed to a widespread activity of the virus (cf. No. 36, p. 66), or where the Wassermann reaction and the signs of disease underwent a profound change for the better under treatment (cf. No. 146, p. 67). These belonged to the category fully described by Léri, and were instances of meningo-vascular syphilis. But we also showed that there was another group of syphilitic amyotrophies exactly analogous in their behaviour to tabes dorsalis, optic atrophy, or the so-called "parasymphilitic" lateral and combined scleroses. For not only do these patients show little improvement under anti-syphilitic treatment, but the Wassermann reaction remains materially unaltered in the cerebrospinal fluid.

Consider such an instance as the following:—

A Case of Muscular Atrophy of Syphilitic Origin, associated with Abnormal Reaction of the Pupils. Positive Wassermann Reaction in the Cerebrospinal Fluid.

Case 198.—F. W., male, married, engineer's assistant; born 1868. In 1888, at the age of 20, this patient became infected with syphilis; he suffered from a chancre for which he was treated for a few weeks only. No manifestations of secondary syphilis followed and he remained in good health. He married in 1893 and three healthy children were born in 1894, 1897, and 1902, and are all alive; his wife has never miscarried.

In 1906, eighteen years after infection, he first complained of pain over the metacarpal of the right thumb and shortly after this the right index-finger dropped. Six months later he came under observation, and since this time has attended regularly at the London Hospital under the care of H. H. In 1908, he was an in-patient at the London Hospital and appeared to be a characteristic example of amyotrophic lateral sclerosis. He showed wasting of both upper extremities, most intense in the muscles of the hands and of the forearms, and greater on the right side than on the left; this wasting affected all the muscles of both upper extremities. Bilateral extensor plantar reflexes were obtained, but no ankle-clonus, and the knee-jerks were not increased. The pupils reacted to light and accommodation.

From 1908 until 1911, when he was admitted again to the London Hospital, the weakness and wasting of the upper extremities had progressed, the tongue became affected and the pupils no longer reacted to light. From 1911 until he received treatment with salvarsan, the condition progressed slowly; since then it has remained stationary.

In 1913 all the muscles of the neck, including the sternomastoids and the trapezii, were greatly wasted. The muscles around both shoulder-joints and the pectoralis major and minor, the serratus magnus and the latissimus dorsi were all intensely wasted. The affected muscles of the neck and shoulder regions showed fibrillary twitchings. Much wasting was present in both arms, more severe in the right than in the left. The muscles of the forearms were also gravely affected, but to a slightly less degree than the muscles of the upper arms. All the small muscles of the hands were atrophied and completely paralysed.

Movements of the right shoulder-joint were impossible; at the left shoulder-joint flexion and extension could be performed but not adduction and abduction. There was some movement at the right elbow and a little greater power at the left elbow. The patient could just flex the wrists on both sides and by means of the flexor sublimis and flexor profundus muscles could incompletely flex the fingers. When the fingers were extended he could just flex the distal phalanges by means of the lumbrical muscles. He could not bring his hands to his mouth unless he locked them together, placed his elbows against his trunk and jerked them up by means of movements of his back.

Except for the musculature of the neck and upper extremities, the other muscles supplied from the spinal cord were relatively well developed. There was no spasticity and no grave weakness of the legs.

The knee-jerks were normal and ankle-jerks were readily obtained. Both plantar reflexes gave an extensor response; on the right side the response was more readily elicited than on the left. The abdominal reflexes were unaffected.

Since 1907 he had suffered no pain, and no disturbance of sensibility could be discovered.

At no time had he experienced any difficulty in holding or passing water.

The movements of the lower portions of the spine were unaffected.

The pupils were unequal and excentric; the right was circular in outline and larger than the left, which was oval; they reacted extremely feebly to light, with a slow contraction, followed by an immediate dilatation, but both reacted well to accommodation.

The tongue showed severe, bilateral, almost symmetrical wasting, and fibrillary twitchings.

The movements of the eyes, jaws, face, palate, and larynx were unaffected.

Vision, hearing, smell, and taste were all normal, and the optic discs and fundi appeared healthy.

He was an extremely intelligent man, and showed no loss of memory, aptitude, or attention. He had never suffered from seizures or attacks of vomiting, and was not subject to headaches.

In January, 1913, the Wassermann reaction was found to be positive in the serum. In February, 1913, he was admitted as an in-patient at the National Hospital, Queen Square, where he was injected with two doses of 0.4 gm. of salvarsan.

On August 2, 1913, at the London Hospital, he was injected with 0.9 gm. of neosalvarsan.

On August 6, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 4.4.0.0.0.}$

He returned for further treatment in December, 1913, and was injected on December 3, on December 4, and again on December 8, with doses of 0.9 gm. of neosalvarsan.

On December 3, 1913, the Wassermann reaction was $\frac{\text{serum } 4.3.0.0.0.}{\text{cs.f. } 4.4.0.0.0.}$

On May 6, 1914, the Wassermann reaction was $\frac{\text{serum } 4.2.0.0.0.}{\text{cs.f. } 4.2.0.0.0.}$ and the cells numbered 3 per cubic millimetre.

Since the beginning of 1913 no new wasting and no fresh manifestations of any sort have developed.

This case corresponded in every detail with the usual description of amyotrophic lateral sclerosis, and yet the defective reaction of the pupils and the character of the Wassermann reaction in the cerebrospinal fluid shows that it belongs to the category of syphilis centralis. It is exactly analogous to a progressive case of tabes dorsalis or any other so-called "parasyphilitic" disease.

It is not difficult to differentiate such a case as this from those where the muscular atrophy is accompanied by other meningo-vascular lesions like No. 36 (p. 66). But we are still doubtful into which category No. 75 should be placed. This was a man, aged 36, who showed all the signs of a muscular atrophy of the upper extremities without any disturbance of sensation. The reflexes were unaffected, the pupils reacted extremely feebly to light, but there were no other abnormal signs pointing to lesions elsewhere in the nervous system.

The Wassermann reaction on April 2, 1913, was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.0.0.}$ with 44 cells per cubic millimetre.

At first sight he is exactly analogous to No. 198, but after treatment with injections of neosalvarsan the atrophy ceased to progress and the strength of the positive reaction in the cerebrospinal fluid steadily diminished until on May 13, 1914, it was $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f. } 4.0.0.0.0.}$ and 3 cells per cubic millimetre.

A Case of Muscular Atrophy of Syphilitic Origin associated with Abnormal Reaction of the Pupils. Positive Wassermann Reaction in the Cerebro-spinal Fluid.

Case 75.—W. H., male, married, messenger; born 1877. He was in the Army in 1896, and again between 1900 and 1908; but although exposed to infection he can remember no venereal disease of any kind. In 1900, whilst in the Army, he had a bad throat lasting a few weeks only which was diagnosed as "diphtheria," but no other manifestations suggesting secondary syphilis.

In 1911 he began to lose power in the middle finger of his right hand. About three months later wasting started in the left arm, and within the space of a year had progressed to such an extent that he was unable to use either upper extremity.

On admission to the London Hospital on March 25, 1913, he was seen to be a well-developed man. All movements were impossible in the right upper extremity below the shoulder-joint and all the muscles, especially those of the hand, showed intense wasting. He could slightly flex the ring-finger of his left hand and evoke a feeble contraction of the flexors of the elbow, but otherwise all muscular power was lost. Movements at the right shoulder-joint were impossible; he could slightly contract the muscles of the left shoulder, but not with sufficient strength to produce any material change in the position of the limb. All the muscles of the neck were weaker than normal and somewhat wasted. There was no spasticity of the legs and the muscles of the trunk and lower extremities were normally developed.

The knee-jerks were brisk, the ankle-jerks were easily obtained, and both plantar reflexes gave a flexor response. The abdominal reflexes were normal. The wrist- and elbow-jerks could not be obtained.

He had suffered no pain, and no disturbance of sensibility could be discovered.

At no time had he experienced any difficulty in holding or passing his water.

Memory, attention and speech were unaffected and he did not suffer from headache, seizures, or attacks of vomiting.

Hearing, smell, taste and vision were normal, and the optic discs and fundi appeared healthy.

All ocular movements were natural. The pupils were unequal, the right larger than the left; both reacted extremely feebly to light with a slow, rhythmic response, but they reacted briskly to convergence and accommodation. The tongue showed no fibrillary tremor and the movements of the face, jaws, palate, and larynx were unaffected.

The blood pressure was 140 mm. of mercury and no abnormal signs were discovered in the heart, lungs, or abdomen. The urine contained neither albumen nor sugar.

On April 2, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.0.0.}$ and the cells numbered 44 per cubic millimetre.

He was injected intravenously with doses of 0.9 gm. of neosalvarsan on April 5, April 12, and April 23, 1913.

He was readmitted for further observation on September 21, 1913, and although no material change had occurred in the manifestations of his nervous disease, his general condition had strikingly improved.

On September 24, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.3.}}{\text{cs.f. 4.3.0.0.0.}}$

On September 24, 1913, he was again injected with 0.9 gm. of neosalvarsan and by May 13, 1914, the Wassermann reaction had become $\frac{\text{serum 4.4.4.3.0.}}{\text{cs.f. 4.0.0.0.0.}}$ and the cells now numbered only 3 per cubic millimetre.

Are we to look upon this patient as an example of syphilis centralis where the process is coming to a natural end, as may happen in tabes dorsalis, or is his muscular atrophy mainly the expression of meningo-vascular changes which have been influenced by treatment?

If both syphilis centralis and syphilis meningo-vascularis are manifestations of the same process in different anatomical structures, it is obvious that there can be no sharp line between them from the clinical aspect. Both can produce exactly the same clinical picture; it is only in those cases where additional signs point to accessory lesions, or where the Wassermann reaction in the cerebrospinal fluid becomes rapidly negative, that we can say with certainty whether or no the lesion is mainly meningo-vascular and can be influenced by drugs circulating in the blood-stream.

Thus, in conclusion, we believe that a form of anytropy exists which is exactly analogous to tabes dorsalis and primary optic atrophy; it may be associated with these conditions, or may occur alone. It is equally a manifestation of the activity of syphilis centralis, where the virus is acting on hypersensitized tissues, bathed in fluids which are only indirectly in connexion with the blood-stream.

§ 4.—*Optic Atrophy.*

Primary optic atrophy occurs so frequently as a complication of tabes dorsalis, that most observers have looked upon it as a manifestation of "parasyphilis." Thus Nonne ([13], p. 174) goes so far as to say that primary optic atrophy is always a sign that the case is one of tabes dorsalis, even if the knee-jerks are present, and he adds that it may exist alone for a long period before the appearance of any other signs. He gives a perfect instance of a woman, whom he had watched for eighteen years, with primary optic atrophy,

and no signs of tabes dorsalis or dementia paralytica had so far appeared.

To this we can add the following instance of a woman who began to lose her eyesight six years before admission to the Hospital. She was blind and showed all the signs of primary optic atrophy without any further evidence of disease of the nervous system.

A Case of Primary Optic Atrophy where the Knee-jerks and Ankle-jerks were normal and there were no signs of Affection of the Posterior Columns of the Spinal Cord.

Case 186.—J. A., female, widow; born 1853. In 1875, at the age of 22, she married her first husband, who died six years later from "asthma and bronchitis"; two out of three children, the issue of this marriage, were alive and well.

In 1892 she was married again to a husband who ultimately developed dementia paralytica and died insane in 1912. In this marriage she had two children, the first of whom, born in 1893, died of "wasting" at three months old, whilst the second, born two years later, was alive and healthy.

In 1905 she began to suffer from pains in the chest, but in view of the large gastric ulcer from which she ultimately died, these pains are of doubtful significance.

In 1907 she began to lose her eyesight. This loss of vision progressed slowly and culminated in 1910 in complete blindness.

When admitted in May, 1913, she was a sallow, anæmic woman, extremely intelligent, but totally blind. She suffered mainly from hæmatemesis and melæna which were due to a chronic ulcer of the stomach.

She showed no loss of memory or attention and had not suffered from any seizures or fits of any kind. Her speech was unaffected.

She was completely blind and the optic discs were in a condition of primary white atrophy. Hearing, smell and taste were unaffected.

The pupils were equal and reacted well to accommodation; they did not react to light in consequence of her blindness. All movements of the eyes, jaws, face, tongue, palate and larynx were performed normally. There was no tremor, no ataxia and she did not become unsteady when her eyes were closed.

No loss of sensation could be discovered to touch, pain or temperature, and she was able to appreciate perfectly the vibrations of a tuning-fork. Recognition of posture and passive movements was unaffected.

The knee-jerks and ankle-jerks were normal and both plantar reflexes gave a flexor response. The sphincters acted normally.

On May 5, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.3.0.0.}{\text{cs.f. } 4.4.3.0.0.}$ and the cells numbered 30 per cubic millimetre.

She died suddenly on May 30, 1913, of hæmatemesis and at the autopsy a large chronic ulcer of the stomach was found which had opened one of the coronal arteries.

The brain and spinal cord showed no signs of gummatous meningitis, but there was slight thickening of the leptomeninges; this was greatest in the neighbourhood of the optic tracts. Both optic nerves were atrophied but showed comparatively little infiltration. The cortex cerebri showed no abnormal changes. The posterior columns of the spinal cord were unaffected, except that, from the level of the 7th cervical segment upwards, a degeneration could be seen on both sides corresponding to a lesion of the 8th cervical nerve-roots. Sections of the 8th cervical spinal ganglion showed this root to be infiltrated. No changes were visible in the Weigert-Pal specimens pointing to *tabes dorsalis* and the other columns of the spinal cord appeared normal. There was no endarteritis or endophlebitis.

Thus it would seem that syphilis can produce degeneration of the optic nerve exactly analogous to the destruction of the posterior columns of the spinal cord in *tabes dorsalis*. Meningo-vascular syphilis may cause optic neuritis (No. 122, p. 16) and subsequent atrophy; but the changes dealt with in this section are manifestations of the activity of syphilis centralis, and they may occur apart from *tabes dorsalis* or any analogous condition.

§ 5.—*Gastric Crises.*

Uncontrollable attacks of vomiting bearing no relation to food are, like optic atrophy, so common a complication of *tabes dorsalis* that we are liable to forget that they are not an essential part of the disease. The gastric crises of *tabes dorsalis* probably arise in several different ways; but one form is obviously associated with irritation of the posterior nerve-roots in the thoracic region of the spinal cord. In these roots run the afferent fibres from the viscera, conducting their impulses to segmental centres in the spinal cord. Thus any inflammatory reaction of these posterior root-fibres in the thoracic region, whether inside or outside the spinal cord, will tend to set up reflex attacks of vomiting accompanied with violent root-pains around the trunk due to the coincident irritation of the somatic afferent fibres of the posterior roots.

In this section we are dealing with those gastric crises only which are accompanied by radicular pains and over-response to painful stimuli somewhere within the territory supplied by the sixth to the tenth thoracic roots. Some acute attacks of vomiting, occurring in *tabes dorsalis*, are not associated with these root-symptoms and, although they are true gastric crises of nervous origin, do not come within the group with which we are dealing.

Obviously any irritation of sufficient persistence and severity in

the lower thoracic region of the spinal cord will be liable to evoke paroxysmal attacks of reflex vomiting. We are so accustomed to associate these gastric crises with irritative destruction of the roots due to *tabes dorsalis*, that other possible causes for their appearance have been neglected. In Chapter III (p. 22) we have called attention to violent attacks of vomiting associated with irritation of the posterior roots by meningo-vascular syphilis; we gave an instance where the Wassermann reaction became negative within six months under the influence of injections of neosalvarsan.

When, however, the attacks are due to irritation of those same visceral afferent fibres by syphilis centralis, as for instance in cases of *tabes dorsalis*, the Wassermann reaction in the cerebrospinal fluid remains materially unaltered. The attacks are quite uninfluenced by the intravenous injections; in fact our experience has been that each injection is liable to be followed by a somewhat severe gastric crisis in patients with syphilis centralis.

Although these gastric crises are usually associated with some signs of affection of the posterior columns elsewhere than in the thoracic region, and the knee- and ankle-jerks are usually absent, this is not always the case. If no other signs are present the differential diagnosis is often very difficult apart from the behaviour of the cerebrospinal fluid. We have, therefore, chosen as our examples two cases where the deep reflexes were unaffected, and no other abnormal signs could be discovered except the defective reaction of the pupils.

The first example (No. 199) was a man aged 40 who, eleven years after infection, began to suffer from intense pain in the epigastric region associated with occasional attacks of vomiting. So severe was the pain that he was admitted under the surgeons as a case of duodenal ulcer. Sensibility to prick, and temperature was diminished over the area of the ninth and tenth thoracic roots on both sides accompanied by great over-reaction to any unpleasant stimulus; there was no demonstrable loss of sensation to cotton-wool. The left pupil did not react to light, but the deep reflexes were normal, and nothing pointed to any affection of the posterior columns of the spinal cord as far as the upper or lower extremities were concerned. The Wassermann reaction which was highly positive in the cerebrospinal fluid, remained entirely unaltered during the six months following treatment.

Our second case (No. 224) was almost identical in every way. The pupils reacted badly to light, but the deep reflexes were unaffected. Here, however, there was no diminution of sensibility, and all

tenderness and "hyperalgesia" disappeared between the attacks. In this patient also the highly positive Wassermann reaction in the cerebrospinal fluid was unaffected by treatment.

A Case of Gastric Crises with Defective Reaction of the Pupils and active Knee- and Ankle-jerks. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which was not affected by Treatment although the Number of Cells was greatly reduced.

Case 199.—A. C., male, married, omnibus conductor; born 1874. This patient contracted syphilis in 1901 at the age of 27; he suffered from a chancre which healed without treatment and was not followed by any manifestations of secondary syphilis.

He married in 1897. His eldest child was born in 1899, the second, born in 1901, died three months later, the third was born in 1902, the fourth in 1903, the fifth in 1905, the sixth in 1906. He had been unhappy in marriage and he and his wife separated in 1908.

His health remained fair until 1908, when he attended at the Royal Ophthalmic Hospital, Moorfields, for some weeks complaining of "iritis." On November 1, 1912, whilst on the top of his 'bus, he was thrown against the side and hurt his left hand; the hand was bruised and did not seem to recover. Whilst still away from work, on December 15, 1912, he suffered from his first vomiting attack. The attack came on suddenly and seemed "like a bad attack of sea-sickness"; it was accompanied by intense pain in the abdomen and back and a "miserable feeling all over." The first attack lasted some twenty-four hours. Between December, 1912, and August, 1913, he suffered from six such attacks. They came on suddenly without warning, and, after lasting a variable period, usually a day and a half, ceased suddenly.

Each attack was more severe than its predecessor and was accompanied by much loss of weight. In December, 1912, he weighed 10 st. 6 lb. (66 kilos), in August, 1913, 8 st. 10 lb. (55 kilos).

He was admitted to the surgical side of the London Hospital on August 11, 1913, with the diagnosis that he was probably suffering from duodenal ulcer. On admission he was a spare man with thin limbs. He was miserable, inattentive and subject to attacks of weeping. His memory was fairly good and his speech unaffected. He slept badly. He had not suffered from headache or seizures. For the first six days after admission he vomited several times every day; these attacks of vomiting were only controlled by the free administration of morphia.

On admission he complained of shooting pains, tightness, and a miserable feeling of the lower abdomen and back, over an area corresponding to the distribution of the 9th and 10th thoracic roots on both sides. This area was tender to pressure and responded excessively to the dragged point of a pin. He said that the point here seemed "dull" and "different" although it "hurt more," and that the hot and cold tubes were "altered" and "not so hot,"

"not so cold"; and yet the sensation evoked by cotton-wool was "the same" over this area as elsewhere over the body. On the extremities there was no sensory loss and the vibrations of a tuning-fork were well appreciated everywhere.

His muscular power was poor, but his gait was unaffected and Romberg's sign was not obtained. There was no ataxia of the hands, no local paresis or atrophy of any group of muscles, and no hypotonia.

The knee-jerks and ankle-jerks were readily elicited and both plantar reflexes gave a flexor response. The abdominal reflexes were unaffected.

He had experienced some difficulty in passing his water and often had to wait for ten or more minutes before the stream would come.

The ocular movements were unimpaired. The pupils were of pin-point size, regular in outline and well centred; the left did not react to even the brightest lights, the right reacted sluggishly; in bright light neither pupil reacted to accommodation, but if he was kept in the dark a slight reaction was obtained. The movements of the face, jaws, palate, larynx and tongue were unaffected. The functions of the special senses were unimpaired and the optic discs and fundi appeared natural.

On August 20, 1913, the Wassermann reaction was

serum	4.4.4.4.0.
c.s.f.	4.4.4.4.0.

 and the cells numbered 40 per cubic millimetre.

On August 15, on August 20, and again on August 24, he was given intravenous injections of 0.9 gm. of neosalvarsan.

After treatment the vomiting ceased, the patient's mental condition brightened, the sensory over-reaction became less and its limits more difficult to define; the patient declared that he felt "better than he had felt for months."

He returned for further treatment and investigation in February, 1914. At this time he was more contented and less worried. He said that since his discharge he had found great difficulty in avoiding alcohol and in keeping "straight." Since his discharge he had suffered from attacks of vomiting lasting about a day, coming on at intervals of about a week or a fortnight and leaving his abdomen sore. His physical state was little altered except that the upper abdominal muscles now appeared wasted and bulged when he lifted his head from the bed, and the plantar responses were no longer definitely flexor.

On February 19, 1914, the Wassermann reaction was

serum	4.4.4.4.0.
c.s.f.	4.4.4.4.0.

 but the cells numbered 4 per cubic millimetre only.

A Case of Gastric Crisis with Argyll-Robertson Pupils and active Knee- and Ankle-jerks. Strongly Positive Wassermann Reaction in the Cerebro-spinal Fluid which was not affected by Treatment.

Case 224.—P. H., male, married, mercantile marine service; born 1883. In the summer of 1911, he began to suffer from apparently causeless attacks of vomiting, unaccompanied by abdominal pain. For the first two months the

attacks came on once or twice a week and lasted two or three days. They started and ended suddenly. Towards the end of the year 1911 the attacks became less frequent; in August, 1912, however, they again became more numerous and of longer duration. For a week or more he would vomit after every meal; this was followed by a period of normal health, succeeded in turn by another attack. At this time the vomiting was effortless and was not preceded by nausea or retching. It was not accompanied by flatulence, pyrosis or indigestion and he was not constipated between the attacks.

On August 28, 1913, a violent attack started which lasted continuously for a fortnight; in this attack for the first time pain became a noteworthy feature; the abdomen in the region of the epigastrium became sore and every few minutes a pain shot from this portion of the abdomen round the trunk into the back. This made him extremely miserable and depressed. During the attack he lost flesh and his weight fell from 11 st. 9 lb. in 1911 to 9 st. 7 lb. in September, 1913, a loss of 30 lb. (or 13½ kilos).

He denied all venereal infection, but admitted exposure as a young man. Whilst abroad in 1900 he suffered from "yellow fever" and also from "cholera." He married in 1909, and in 1911 a child was born which is healthy.

On September 13, 1913, he was admitted to the London Hospital for operation under the care of Mr. James Sherren, complaining of attacks of vomiting and an irritable feeling in the upper part of the abdomen and back; he said he felt worried and was mentally very depressed.

No abnormal physical signs were discovered in the abdomen, heart, arteries or lungs. A test breakfast of toast and tea showed the presence of 0.08 per cent. free hydrochloric acid and a total acidity of 42. Radiological examination of the stomach showed that it was not dilated and emptied itself rapidly.

When transferred to the medical side he was loquacious, introspective and inattentive. His memory was somewhat defective, but he gave his history clearly. He said that he forgot little details of his work, and that his "memory was not what it was." His speech was unaffected and headache was not a noticeable feature. After admission he vomited many times; the attacks of vomiting were sudden and bore no relation to food, but were accompanied by much abdominal pain with superficial and deep tenderness of the upper abdomen on both sides. He vomited many times each day for eight consecutive days. He had suffered from no other form of paroxysmal attacks or from epileptiform seizures.

The pupils were unequal, the right much wider than the left; the left just flickered on stimulation with intense lights, whilst the right showed no reaction, but both reacted well to accommodation. No other abnormal signs were discovered in the territory of the cranial nerves.

Taste, smell, hearing and vision were unaffected, and the fundi showed no abnormal appearances.

Motion was completely unaffected and no disturbance of sensibility was present except during the attacks and for three days afterwards. Posture and

passive movement and the vibrations of the tuning-fork were well recognized on both legs. During the attacks of vomiting the areas of skin corresponding to the peripheral distribution of the sixth, seventh, eighth, and ninth thoracic nerve-roots on both sides became tender and over-reacted to pinching and the dragged point of a pin, but over these areas no sensory loss of any kind could be discovered.

The knee-jerks and ankle-jerks were readily obtained and the plantar reflexes on both sides gave a flexor response. The abdominal reflexes and the wrist- and elbow-jerks were normal.

He suffered from no trouble in holding or passing his urine or motions.

The urine contained a trace of albumen and a small quantity of pus, but the quantity secreted and the specific gravity were normal.

The Wassermann reaction on September 19, 1913, was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs. f. } 4.4.4.0.0.}$

He was injected on September 24, October 1, and October 13, 1913, with doses of 0.9 gm. of neosalvarsan. After each injection he suffered from a violent gastric crisis, lasting about forty-eight hours, with slight pyrexia to 100° F. (38.3° C.). The quantity of urine excreted fell from 42 oz. to 22 oz. on an average. As soon as the vomiting ceased he rapidly regained the weight which he had lost during the attack.

He was readmitted for investigation on April 17, 1914. The signs of disease were unchanged and, although the attacks were as numerous and severe as before, his general condition between them had improved greatly.

On April 23, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 4.4.4.1.0.}$ and the cells numbered 13 per cubic millimetre.

He was treated with 0.9 gm. of neosalvarsan on April 21, 1914. After this injection a violent "gastric crisis" set in and lasted until May 1. On April 23 he vomited three times, on the 24th six times, on the 25th six times, on the 26th twice, on the 27th six times, on the 29th four times, on the 30th once, and on May 1 once. The whole abdomen between the peripheral distribution of the 6th thoracic and the 1st lumbar nerve-roots on both sides was tender and reacted excessively to the dragged point of a pin; this area of tenderness gradually disappeared and by May 1 had almost entirely gone. During the attack he took hardly any food, he wasted rapidly and cried out for morphia. Whenever he came round from the effect of the drug, he was extremely miserable and immediately complained of a feeling of sickness, retched and vomited. The attack ended suddenly and left him extremely weak.

By May 6, he felt well again and was injected with 0.9 gm. of neosalvarsan. On this day and again on May 9 he received a similar dose; neither injection was followed by any ill-effect.

§ 6.—*Epileptic Manifestations.*

Fournier ([4] p. 238) called attention to a form of epilepsy liable to appear many years after syphilitic infection, which was entirely refractory to anti-syphilitic treatment. This he believed to be a

manifestation of "parasyphilis." Nonne ([13] p. 284) entirely agrees with this description and accepts "parasyphilitic" epilepsy as a condition comparable to tabes dorsalis and dementia paralytica. He carefully differentiates it, on the one hand from cerebral syphilis, and on the other from the seizures which may herald the early stages of dementia paralytica.

But all authorities agree that "gummatosis" affecting the cerebral cortex may produce a condition which cannot be materially improved by anti-syphilitic remedies; clinically it cannot be differentiated from this "parasyphilitic" epilepsy, except by the behaviour of the Wassermann reaction in the cerebrospinal fluid. For, as a rule, the cerebrospinal fluid in cases of chronic meningo-vascular syphilis of the cortex yields a negative reaction, if there are no spinal or bulbar complications; but any case diagnosed as "parasyphilitic" epilepsy must follow the rules we have laid down and give a positive reaction in the cerebrospinal fluid, which is not materially affected by anti-syphilitic treatment.

We have seen one case only (No. 66) which fulfilled these conditions. The disease arose on a basis of a juvenile infection and is interesting from the presence of Argyll-Robertson pupils. It illustrates the long duration of the disease and the persistence of the positive Wassermann reaction in the cerebrospinal fluid in spite of treatment. At the end of over two years the strength of the reaction was almost the same as on the first observation.

A Case of Epilepsy in a Patient with Juvenile Syphilis. The Wassermann Reaction was Positive in the Cerebrospinal Fluid and the Cells were in excess. Treatment improved her General Condition, but did not stop the Fits or materially change the Strength of the Wassermann Reaction.

Case 66.—F. G., female, single; born 1889. This patient has been under the care of H. H. since 1904 suffering from epileptiform attacks. In 1900, at the age of 11, she developed fits, which have continued ever since in spite of treatment. The attacks come on without warning, she passes water, falls, and has not infrequently hurt herself. Throughout she is completely unconscious, and she sleeps after the attack. Usually two or more fits occur in rapid succession.

There is no family history of epilepsy. Her mother married in 1878. Of this marriage there have been (i) a child born in 1879, who died at the age of 14 months of "consumption of the bowels"; (ii) a child born in 1881, who died aged 12 months of "scarlatina"; (iii) a healthy female, born in 1885, now married, with a healthy child, born in 1911; (iv) a healthy male, born May, 1887; (v) the patient, born April, 1889; (vi) a male born in 1891, living and healthy; (vii) a child who died at the age of 12 months of "summer diarrhoea"; and (viii) a child who survived and is healthy, born in 1895.

The patient was a full-time, healthy child, born with a breech presentation after a difficult labour.

In 1890, at the age of 18 months, she developed a syphilitic rash and was treated for eight months with mercury by the mouth. Under this treatment she developed into a "fine healthy child."

Before the onset of the nervous manifestations, her only illness was an attack of measles in 1897.

In 1897, at the age of 10, she reached Standard iv; then she began to "go wrong." She became restless, irritable, and clumsy in action and subsequently began to suffer from epileptiform attacks.

In 1903 she attended the ophthalmic department of the London Hospital under the care of Mr. Roxburgh for interstitial keratitis, and was transferred by him to the care of Dr. Head.

She is short and broad, 4 ft. 10 in. (146 cm.) in height with a narrow forehead and pegged teeth. Scars are visible at the angles of the mouth and she has the characteristic appearances of a case of juvenile syphilis.

Her attention and memory are poor, but she shows no gross signs of dementia. Her speech is unaffected, and excepting after an attack, she is not liable to headaches or vomiting.

She is somewhat deaf. The corneæ show faint nebulae, but the fundi appear natural.

The pupils are usually equal and of fair size, but they do not react to light; they react well to accommodation. The face is expressionless and the tongue on protrusion comes out straight and is held steadily.

The knee-jerks and other reflexes including the plantars are normal, except after a series of convulsions.

Motion, sensation and the action of the sphincters are entirely unaffected.

In September, 1911, with "heart antigen" the Wassermann reaction was $\frac{\text{serum } 0.0.0:0.0.^1}{\text{cs.f. } 4.2.1.0.0.}$ and the cells were in excess. At this time she was thought to be a case of juvenile dementia paralytica and was not injected with salvarsan.

On June 4, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 4.4.4.4.0.}$ and the cells numbered 40 per cubic millimetre.

On June 6, 1913, she was given 0.9 grm. of neosalvarsan intravenously, and similar doses were administered on the 13th and 18th of that month.

After the injections her general condition improved and for the first time she began to menstruate regularly. The treatment, however, had no effect on the nature or the frequency of the attacks.

On December 4, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.1.0.0.}{\text{cs.f. } 4.4.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

¹ This is the only occasion in this paper when we have quoted a Wassermann reaction obtained with this antigen. In all other instances, including the other estimations in this patient, the technique was that laid down by Fildes and McIntosh [3].

TABLE F.—TO SHOW THE ABSENCE OF CHANGE IN THE WASSERMANN REACTION AFTER TREATMENT IN CASES OF SYPHILIS CENTRALIS.

No. of case	Before treatment	After treatment	Intervening period	Treatment
DEMENTIA PARALYTICA.				
20 (Autopsy) ..	<u>4.4.4.3.1.</u> 4.4.4.4.1.	<u>4.4.4.3.2.</u> 4.4.4.2.0.	45 weeks	3 doses of 0.9 grm. of neosalvarsan
32 (p. 92) ..	<u>4.4.4.2.1.</u> 4.4.4.3.2.	<u>4.4.4.4.0.</u> 4.4.4.2.0.	63 "	2 doses of 0.6 grm. of salvarsan
90 (Autopsy) ..	<u>4.4.4.4.2.</u> 4.4.4.4.0.	<u>4.4.4.4.4.</u> 4.4.3.0.0.	23 "	3 doses of 0.9 grm. of neosalvarsan
200 (p. 95) ..	<u>4.4.4.4.3.</u> 4.4.4.4.4.	<u>4.4.4.4.4.</u> 4.4.4.4.4.	55 "	4 doses of 0.9 grm., 1 of 0.2 grm. and 3 of 0.3 grm. of neosalvarsan and 4 intrathecal injections of 10 c.c. of "salvarsanized serum"
230 (Autopsy) ..	<u>4.4.4.4.4.</u> 4.4.4.4.4.	<u>4.4.4.4.4.</u> 4.4.4.4.4.	15 "	3 doses of 0.9 grm. of neosalvarsan
JUVENILE DEMENTIA PARALYTICA.				
197	<u>4.4.4.4.4.</u> 4.4.4.2.0.	<u>4.4.4.4.0.</u> 4.4.4.4.0.	40 weeks	4 doses of 0.6 grm. of neosalvarsan
TABES DORSALIS.				
37 (p. 107) ..	<u>4.4.2.0.0.</u> 4.4.3.1.0.	<u>4.4.4.2.0.</u> 4.4.2.0.0.	47 weeks	3 doses of 0.9 grm. of neosalvarsan
142	<u>4.4.4.0.0.</u> 4.4.4.0.0.	<u>4.4.4.4.2.</u> 4.4.1.0.0.	77 "	2 doses of 0.9 grm. of neosalvarsan
150	<u>4.4.4.4.2.</u> 4.4.3.0.0.	<u>4.4.4.4.4.</u> 4.4.1.0.0.	47 "	3 doses of 0.9 grm. of neosalvarsan
MUSCULAR ATROPHY.				
198 (p. 110) ..	<u>4.4.2.0.0.</u> 4.4.0.0.0.	<u>4.2.0.0.0.</u> 4.2.0.0.0.	41 weeks	2 doses of 0.4 grm. of salvarsan and 4 doses of 0.9 grm. of neosalvarsan
75 (p. 113) ..	<u>4.4.4.4.4.</u> 4.4.4.0.0.	<u>4.4.4.3.0.</u> 4.0.0.0.0.	58 "	4 doses of 0.9 grm. of neosalvarsan
GASTRIC CRISES.				
199 (p. 118) ..	<u>4.4.4.4.0.</u> 4.4.4.4.0.	<u>4.4.4.4.0.</u> 4.4.4.4.0.	29 weeks	3 doses of 0.9 grm. of neosalvarsan
224 (p. 119) ..	<u>4.4.4.4.4.</u> 4.4.4.0.0.	<u>4.4.4.4.3.</u> 4.4.4.1.0.	31 "	3 doses of 0.9 grm. of neosalvarsan
"PARASYPHILITIC" EPILEPSY.				
66 (p. 123) ..	<u>4.4.2.0.0.</u> 4.4.4.4.0.	<u>4.4.1.0.0.</u> 4.4.0.0.0.	26 weeks	3 doses of 0.9 grm. of neosalvarsan

[B] THE EFFECT OF TREATMENT ON THE WASSERMANN REACTION IN SYPHILIS CENTRALIS.

It is universally recognized that syphilis centralis, in its acute forms, tends to produce a strongly positive reaction in the cerebrospinal fluid, and throughout the previous half of this chapter we have given many instances in support of this belief.

This positive reaction is not materially affected by doses of neo-salvarsan sufficient, in cases of meningo-vascular syphilis (Chapter IV, p. 84), to be capable of converting a positive into a negative reaction in the cerebrospinal fluid within a few months.

We have gathered together fourteen cases of the various forms assumed by syphilis centralis, to form Table F, and it will be evident how little change occurs after treatment. In a few cases, such as those of tabes dorsalis and muscular atrophy, the positive reaction in the cerebrospinal fluid is occasionally slightly less strong in the later examination; but there is nothing to show that this was the direct and immediate result of the treatment. We have put together, on Table G, four cases of tabes dorsalis where no anti-syphilitic treatment of any kind was given; of these two showed the same slight diminution in the strength of the positive Wassermann reaction in the cerebrospinal fluid.

TABLE G.—TABES DORSALIS.

No. of case	First observation	Subsequent observation	Intervening period	Treatment
30	4.1.0.0.0.	4.0.0.0.0.	79 weeks	None.
	4.4.4.4.0.	4.4.4.0.0.		
58	4.3.1.0.0.	4.4.4.1.0.	106 "	" "
	4.4.4.0.0.	4.4.4.2.0.		
70	4.4.4.2.0.	4.4.4.4.4.	81 "	"
	4.3.0.0.0.	4.4.0.0.0.		
131	4.3.2.1.0.	4.4.4.4.4.	114 "	"
	4.4.4.3.1.	4.4.0.0.0.		

We believe that syphilis centralis is the reaction of the hypersensitized neuroglia and essential tissues of the nervous system to the activity of the syphilitic virus. In many cases this tissue reaction tends to come to an end with time (p. 102), and provided the patient is not killed by the severity of the active disease, he may settle down into a case of chronic degeneration of certain parts of the nervous

system. His signs and symptoms are due to the after-effects of the tissue reaction and not to any active process. The Wassermann reaction in the cerebrospinal fluid also tends slowly to become negative and we therefore look upon the slight diminution in strength of the positive reaction in some of the cases on Tables F and G as further evidence of this tendency for the active process to die out in the tissues of the central nervous system.

CHAPTER VI.—MIXED FORMS.

We have put forward the view that there is no essential difference pathologically between the nature of meningo-vascular and central syphilis; both are due to the action of the virus on tissues already rendered hypersensitive to a varying degree. The only difference lies in the site of the lesion, and consequently in the character of the tissues attacked. Moreover, the meninges and vessels are exposed to the action of drugs in the circulatory system, whilst the essential elements of the brain and spinal cord are only indirectly affected by the contents of the blood-stream.

If these views are correct, it is obvious that cases must exist where the foci of spirochaetosis affect the meninges, the vessels and the essential structures of the nervous system at the same time. Such cases would show features reminiscent of the behaviour on the one hand of syphilis meningo-vascularis, on the other of syphilis centralis. These we speak of as "mixed forms."

Thus, for instance, No. 159, when he first came under our care, showed signs pointing to basal meningitis and disease of the cerebral vessels; for, in addition to his mental instability, a well-marked nystagmus was present, and the right half of the palate was paretic. But, although these signs disappeared under treatment, the positive Wassermann reaction in the cerebrospinal fluid remained uninfluenced, and his general condition steadily deteriorated. It is interesting to notice in this case that the symptoms of disease of the central nervous system came on within three years of infection.

The second case (No. 280) was thought to be one of dementia paralytica, in spite of the short period that had elapsed since infection. Speech was affected, face, tongue, and hands were tremulous, and the patient had suffered from several seizures. He had been treated with mercury and with intravenous injections of salvarsan before he came under our care in August, 1912; but his Wassermann reaction was completely positive in the cerebrospinal fluid.

He improved greatly under treatment, and is now able to take part in the ordinary occupations of daily life. His memory is good, and he can even solve complicated problems in calculation. But his speech is still affected, and a good deal of tremor remains in the face and tongue. At the same time the Wassermann reaction in the cerebrospinal fluid is still almost completely positive, and shows no material change in spite of energetic anti-syphilitic treatment.

In No. 125 our third instance of these mixed forms, the obvious root affections, accompanied at one time by herpes zoster, pointed to active disease of the meninges. On the other hand, the absent knee-jerks, ataxy, and other signs of profound affection of the posterior columns pointed to central disease. The patient improved greatly under treatment, and at first the highly positive Wassermann reaction in the cerebrospinal fluid yielded somewhat to treatment. But at the end of over twelve months he still gave a strongly positive reaction in the cerebrospinal fluid; the root-symptoms and weakness in the legs had disappeared, but he now exhibited all the signs of tabes dorsalis. Here, then, was an instance where one aspect of the disease showed great improvement, but the signs of deeper affection of the nervous system remained unaltered.

A Case of Syphilis of the Central Nervous System appearing Three Years after Infection. A Strongly Positive Wassermann Reaction and Great Pleocytosis in the Cerebrospinal Fluid which were not influenced by Treatment.

Case 159.—W. G. T., male, single, surveyor; born 1878. In 1908, at the age of 30, this patient contracted a "running"; at first this was thought to be a simple gonorrhœa, but a few months later he suffered from a series of bad throats and was then treated regularly for eighteen months with mercurial pills.

From 1908 until the spring of 1911 his health was fairly good. Then his memory began to fail and he found that he was no longer able to do his work up to his old standard and that he was easily worried with the details of business. In January, 1912, insomnia became troublesome and he suffered from a "continual muzziness in the head," "a sort of headache at the back of the eyes with a buzzing noise and discomfort in the ears." He became more worried, more emotional and began to lose flesh. In June, 1912, he went to camp with the Territorials: on his return he had a "complete nervous breakdown" with depression accompanied by neurasthenic symptoms. He became unable to think consecutively and felt unequal to any but routine work. During the next six months he remained in much the same condition; the only new symptom which developed during this time was some difficulty in starting micturition.

He first came under our observation on January 18, 1913. On admission

memory, especially technical memory, was defective; he was depressed and introspective. His attention was good and his speech unaffected. He complained of noises in the head and of a feeling of fulness which was not accompanied by any pressure-tenderness of the scalp. He had suffered from no seizures and from no attacks of vomiting.

Hearing, smell, taste, and vision were unaffected and the optic discs and fundi appeared healthy.

A well-marked nystagmus was present; this was best observed when the patient looked to the extreme left and was more noticeable in the left eye than in the right. The pupils were equal and well centred; both reacted to light and accommodation; on the right side, however, the reaction was badly sustained. There was no diplopia or ptosis and the facial movements were natural. On phonation the uvula was drawn up to the left, but the movements of the tongue and larynx were unaffected and there was no wasting of the trapezius and sternomastoid muscles.

The gait and movements of the hands were unaffected. There was no alteration in the muscular tone of the extremities and no local muscular wasting was present.

The patient complained of no spontaneous pains in the trunk and no interference with sensation was discovered.

The knee-jerks and ankle-jerks were readily obtained, but on the right side the plantar reflex gave an extensor, on the left a flexor response. The abdominal reflexes and the wrist- and elbow-jerks were natural.

Whilst under observation he experienced no difficulty in holding or passing water; but before his admission he had had difficulty in starting the act of micturition and occasionally he had wetted himself.

On January 22, 1913, the Wassermann reaction was serum 4.4.4.3.0.
cs.f. 4.4.4.4.1.
and the cells numbered 50 per cubic millimetre.

He was injected on January 25, January 31, and February 5, 1913, with doses of 0.9 gm. of neosalvarsan.

After this treatment he improved considerably, regained confidence and went back to his old employment. He returned for further investigation in October, 1913. At this time his physical state was closely similar to that shown in the previous January, except that the nystagmus had disappeared and his palate moved normally. On October 14, 1913, the Wassermann reaction was serum 4.4.4.4.0.
cs.f. 4.4.4.4.4.
and the cells numbered 40 per cubic millimetre.

He was injected with 0.9 gm. of neosalvarsan on October 24, and again on November 14 and November 18, 1913.

On June 8, 1914, he stated that he was more easily tired. He had lost his employment, but had just returned from training in camp. There he acted as sergeant and led his battery, but was obliged to go into hospital, at least on one occasion, "because he felt queer." His speech was now affected and there was much tremor of the face and lips. His handwriting was only slightly

affected. All his reflexes, superficial and deep, were now normal. His pupils reacted sluggishly to light, the right better than the left. The palate moved normally. He had no difficulty with micturition.

The Wassermann reaction on June 10, 1914, was serum 4.4.4.4.2.
cs.f. 4.4.4.4.4.
 and the cells were 38 per cubic millimetre.

On June 9, 1914, he was given 0.9 gm. of neosalvarsan without subsequent rise of temperature or any immediate ill results. On June 11, he was given a similar dose. Eight hours later, without rise of temperature or other signs of reaction, he became muddled, looked wildly around the ward, lost his power of counting money and ordered the patients about in a lordly manner. This change lasted until June 14, when it passed away, leaving him in the condition in which he was admitted.

A Case where Signs and Symptoms resembling those of Dementia Paralytica came on within four and a half years of Infection in a man aged 28. The Condition of the Patient improved greatly under Treatment, although the Wassermann Reaction in the Cerebrospinal Fluid remained almost Completely Positive.

Case 280.—V. W., single; born 1884. In March, 1906, he was infected with syphilis and suffered from a chancre, followed by sore throats, but from no other symptoms. He took mercury by the mouth for two and a half years.

In June, 1910, he suddenly fell unconscious in the street, and was convulsed. After this he received a series of injections of mercury cream into the buttock.

On September 14, 1910, he consulted an ophthalmic surgeon, who found his left pupil inactive to light, whilst the right reacted well. This remained constant for many months and as the Wassermann reaction in his serum was positive he was injected with 0.3 gm. of salvarsan on April 13, 1911, 0.4 gm. on April 18, and 0.6 gm. on May 19.

He was operated on for piles on August 15, 1911, so clumsily that a stricture of the rectum was produced, associated with inability to hold his motions from damage to the sphincter ani.

On December 29, 1911, he was again injected with 0.6 gm. of salvarsan.

He was admitted to the Naval Hospital, in January, 1912, because of the trouble with his rectum consequent on the operation. Whilst there he suffered from transitory loss of speech, and on several occasions his arms and legs became "numb and useless."

During June, 1912, he had a second attack in which he fell and became unconscious.

When he first came under our care in August, 1912, his memory was extremely defective, and he was confused; he could not remember dates, muddled the years, and had forgotten the ships in which he had served. Although very highly educated he could not multiply, and found great difficulty with figures. His writing was tremulous, syllables were omitted

and words misspelt, when he wrote to dictation. Speech was thick, slurred and tremulous.

He walked slowly, but there was no ataxy of upper or lower extremities. His hands were tremulous.

The right pupil reacted sluggishly, if at all, to light, and tended slowly to contract and dilate independently of stimulation. It was smaller than the left pupil, which now reacted normally. There was no ocular paralysis, diplopia or nystagmus. The face was flattened; lips and tongue were tremulous.

The knee-, ankle-, and wrist-jerks were exaggerated; no ankle-clonus could be obtained and both plantar reflexes gave a flexor response.

Sensation was not disturbed, vision, hearing and smell were unaffected and both optic discs were normal.

The sphincters now reacted normally, but he was extremely careless about cleansing himself after passing a motion.

His Wassermann reaction on August 8, 1912, was $\frac{\text{serum 4.4.4.4.4.}}{\text{cs.f. 4.4.4.4.4.}}$

On November 26, 1913, he was admitted to the London Hospital, in much the same condition except that both pupils now reacted to light, and the tremor of the face and tongue was less evident. His mental state had considerably improved. The Wassermann reaction was $\frac{\text{serum 4.4.4.4.4.}}{\text{cs.f. 4.4.4.4.4.}}$ and 14 cells per cubic millimetre.

He was injected on November 26, 1913, with 0.9 gm. of neosalvarsan, On February 24 and 26, 1914, he received two doses of 0.9 gm. of neosalvarsan.

Since November, 1913, his symptoms have steadily improved. He now (June, 1914) spends most of his time yachting and his golf handicap is down to 12. Memory has greatly improved, and he is no longer irritable or emotional. Coarse tremor of the lips and tongue is still present but his speech has considerably improved. Both pupils react sluggishly to light; the right is now larger than the left. No other abnormal signs can be discovered. But in spite of this improvement in symptoms, the Wassermann reaction is $\frac{\text{serum 4.4.4.4.1.}}{\text{cs.f. 4.4.4.4.3.}}$ and 9 cells per cubic millimetre.

A Case of Ataxy with much loss of Sensation in both Lower Extremities and Argyll-Robertson Pupils. Loss of all Reflexes superficial and deep below the Groins. Herpes Zoster. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which became slowly reduced after Intensive Treatment.

Case 125.—F. P., male, married, coachman; born 1881. In 1902, this patient contracted a "running" for which he received no treatment. At no time had he suffered from any sore or rash, but some time later he began to complain of bad throats which lasted "a few months."

He married in 1906 and his wife has had two children, born in 1907 and 1910, and no miscarriages.

In September, 1912, he developed an "influenza," in which he suffered from running from the nose and eyes, pains all over and low spirits. After this attack he never "seemed himself." About the middle of October, 1912, he first experienced difficulty in starting the act of micturition, which ended in incontinence of urine from overflow. Towards the end of October he began to complain of intense, dull, heavy pains in the legs and calves. The pains were worse in the left leg than in the right, and were always worse at night than by day. Then his arms became affected with a sort of "cramp" which kept him from using his hands. On November 16, 1912, he took to his bed. On November 20, on attempting to get out of bed he found that he was totally unable to stand. After this date he completely lost sensation in both lower extremities and control over his sphincters.

On December 8, 1912, when admitted to the London Hospital, the patient was a pale, thinly covered man. On the front of the shins were thin tissue-paper scars. The right pillar of the fauces was adherent to the back of the pharynx and both pillars were much scarred. No scar could be found on the penis.

Memory, attention and speech were little affected. He complained of no headache. He had suffered from no seizures or attacks of vomiting.

The movements of the eyes were normal. The pupils were of pin-point size, equal and well centred; neither reacted to the most intense light, but both reacted slightly to accommodation and convergence. In the territory of the cranial nerves no other abnormal signs were present.

The alignment of his fingers and hands was good. He could not stand, but could just move his legs. All the muscles of the lower extremities were flaccid and the calves were wasted, although the thighs were fairly developed.

He complained of spontaneous shooting pains in the legs, and of a tight girdle sensation just below the level of the umbilicus. Over the areas of skin supplied by the eleventh and twelfth thoracic nerve-roots the patient was tender and reacted excessively to the dragged point of a pin. There was much loss to all sensory tests below the level of the groins. The loss to pain, to heat and to cold was greater on the right leg than on the left. Ice and water at 50° C. could be distinguished on both legs, but he was uncertain in his answers to the intermediate degrees of temperature, more especially to those between 20° C. and 40° C. The impairment to painful stimuli affected both pressure-pain and the painful aspect of the prick of a pin. His answers to examination with the tuning-fork and to the tests for posture and passive movement were extremely bad; they were worse on the left leg than on the right, yet whenever any answer was obtained it was correct. The contact of cotton-wool was appreciated on both legs, but there was more uncertainty on the right than on the left.

The knee-jerks and ankle-jerks were completely abolished, and no plantar responses could be obtained to stimulation of the soles of the feet or the front of the ankles and shins. The upper and lower abdominal reflexes were obtained, but the cremasteric reflexes were abolished. The wrist- and elbow-jerks were readily elicited.

On admission, retention of urine necessitated the use of a catheter; on the sixth day after admission he began to pass urine naturally.

No abnormal physical signs were discovered in the heart, lungs, abdomen or urine.

On December 11, 1912, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.4.}}{\text{cs.f. 4.4.4.4.3.}}$ and the cells numbered 5 per cubic millimetre. He was injected with doses of 0.9 gm. of neosalvarsan on January 4, January 14, and again on January 22, 1913.

On February 7, 1913, he was discharged from Hospital. At this time he had little or no knowledge of where his legs were, he could not walk and could only stand with difficulty.

He was readmitted for further treatment on April 21, 1913. At this time he was able to walk. He was extremely ataxic, more especially with the left leg and Romberg's sign was present. The knee-jerks, ankle-jerks and the plantar reflexes could not be obtained. He complained of precipitancy in micturition and of shooting pains in the old tender area (eleventh and twelfth thoracic nerve-roots) and also in the arms and axillæ. Hyperalgesia was present over the distribution of the third, tenth, and eleventh thoracic roots on both sides. There was still much sensory loss on both lower extremities to all tests except cotton-wool.

On April 23, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.4.}}{\text{cs.f. 4.4.4.0.0.}}$ and the cells numbered 3 per cubic millimetre. He was

injected on April 25, 1913, with 0.12 gm. of neosalvarsan.

"	"	"	29,	"	"	0.15	"	"	"
"	"	May	2,	"	"	0.15	"	"	"
"	"	"	5,	"	"	0.3	"	"	"
"	"	"	9,	"	"	0.3	"	"	"
"	"	"	13,	"	"	0.3	"	"	"
"	"	"	16,	"	"	0.3	"	"	"
"	"	"	19,	"	"	0.3	"	"	"
"	"	"	23,	"	"	0.3	"	"	"
"	"	"	27,	"	"	0.3	"	"	"

making in all 2.52 gm.

On September 1, 1913, he developed herpes zoster of the 9th thoracic root on the left side (*vide* fig. 2, p. 24).

On September 7, 1913, the Wassermann reaction was $\frac{\text{serum 4.4.4.4.0.}}{\text{cs.f. 4.4.2.0.0.}}$

He was injected with 0.9 gm. of neosalvarsan on September 8, 1913.

After this treatment the improvement in function continued, but the Argyll-Robertson pupils, the absence of the knee-jerks, ankle-jerks and of the plantar reflexes persisted; and up to the present time (June, 1914) severe sensory loss still exists in both lower extremities, greater to pain, heat and cold on the right side and to posture, vibration and tactile discrimination on the left. He has never regained full control over his sphincters.

On January 29, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.}{\text{cs.f. } 4.4.4.0.0.}$ and the cells numbered 1 per cubic millimetre.

On June 10, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 3.0.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

He now walks with much greater security, but the physical signs of nervous disease remain unchanged.

We could give other instances of these mixed forms where the disease attacks meninges, vessels, and deep structures simultaneously; but we have selected these three examples because of the diversity of their clinical symptoms and because they had all been subjected to unusually energetic treatment, more than sufficient to cause a profound change in the Wassermann reaction of the cerebrospinal fluid, had they been instances of uncomplicated meningo-vascular syphilis.

Thus we believe there are cases where the spirochætes affect directly all the various structures which go to make up the central nervous system, meninges, vessels, neuroglia, and nerve elements. Such patients may show considerable improvement under treatment, but the strength and character of the Wassermann reaction will either undergo no material alteration, or will change extremely slowly compared with an otherwise uncomplicated case of meningo-vascular syphilis. These are instances of combined meningo-vascular and central syphilis in the same patient.

CHAPTER VII.—GENERAL CONCLUSIONS.

In previous chapters we have described the behaviour of the Wassermann reaction under the various clinical conditions produced by syphilis of the central nervous system. But before passing on to the final detailed summary of our results it will be well to review certain more general conclusions at which we have arrived.

The first lesson we have learnt is that clinical signs reveal the site of the lesion but not the nature of the process which has produced it. It is, in many cases, impossible by bedside examination, however careful, to determine whether the patient is suffering from dementia paralytica or syphilitic "encephalitis." Were both conditions of equally fatal prognostic import this question would be a purely academic one. But we have given examples to show that if the patient is suffering from the cerebral form of meningo-vascular syphilis he may be profoundly improved by treatment, whereas in dementia paralytica he is doomed to inevitable and progressive mental decay. Numbers of persons

suffering with cerebral syphilis are condemned to die untreated because they are thought to be suffering from "general paralysis," whereas in reality they are examples of a curable disease.

The treatment of syphilis by modern therapeutic measures is so expensive and troublesome that few inmates of our Asylums and Workhouse Infirmaries receive adequate injections of neosalvarsan or even effective mercurial treatment. No one wastes time and money on persons supposed to be obvious cases of "general paralysis," and we have received letters from medical officers in answer to our inquiries about some patient expressing wonder that we should "take so much trouble over such a straightforward case of general paralysis."

In the same way a single clinical examination fails to reveal the nature of a case of muscular atrophy, unless the pupils happen to be affected or some other sign is present pointing to its syphilitic origin. We cannot say whether the disease can be arrested, or even perhaps cured, until we have watched the effect of efficient treatment on the signs and symptoms and on the Wassermann reaction in the cerebro-spinal fluid.

Again we have shown that "gastric crises" are not of necessity a sign of tabes dorsalis. Any subacute irritation of the fibres of the thoracic posterior roots, whether inside or outside the substance of the spinal cord, may lead to periodic attacks of uncontrollable vomiting. The diagnosis of tabes dorsalis has to be made, not on the character of these attacks or the changes in thoracic sensibility, but on the additional signs of disease in the posterior columns.

But even when we have reason to believe that the posterior columns of the spinal cord are affected as the result of syphilis, we cannot necessarily diagnose tabes dorsalis in every case. Interference with the functions of these columns is not always due to a systemic reaction but may be secondary to vascular changes such as occur habitually in syphilis meningo-vascularis. Treatment and observation of the behaviour of the Wassermann reaction in the cerebrospinal fluid alone will reveal whether we are dealing with changes in the posterior columns secondary to vascular disease or with that systemic reaction to the virus which forms the essential lesion in tabes dorsalis.

A second lesson to be learnt from this research is that the signs and symptoms of syphilis of the central nervous system do not of necessity differ in the various stages of the disease. Two patients may be attacked for the first time with identical nervous manifestations;

yet the one is obviously in the secondary stage, three months after infection, whilst the other was infected twenty-five years before. As far as syphilis of the nervous system is concerned, we have no occasion to speak of "secondary" or "tertiary" or "parasymphilitic" manifestations. The lesions of cerebrospinal syphilis are produced by the reaction of the meninges, the vessels, the neuroglia and the essential elements of the nervous system, to the activity of the *Spirochæta pallida*. The clinical picture expresses the situation of this tissue-reaction, and signs and symptoms will remain the same whenever identical structures are attacked.

Throughout this work we have attached much importance to the behaviour of the Wassermann reaction in the cerebrospinal fluid as the result of treatment. We have gone so far as to suggest that when this reaction can be changed from positive to negative within a few months the pathological changes are mainly in the meninges and vessels. On the other hand should the cerebrospinal fluid remain essentially unchanged in its reaction in spite of identical treatment, we believe that the virus is exercising its activity on parts remote from the direct influence of the blood-stream.

Such a hypothesis, however, depends on two purely empirical procedures. For firstly we have given no facts to show that more energetic treatment, even with neosalvarsan, would not convert a positive into a negative reaction in the same time. We are only justified in stating that the doses we have habitually administered (0.9 gm. of neosalvarsan intravenously) do not materially change the reaction within six months. Secondly, the Wassermann reaction is itself a purely empirical procedure and we do not yet know all the factors which lead to changes in its strength and character.

It is quite impossible to base any pathological theory on the changes produced in this empirical reaction by a purely arbitrary therapeutic procedure. A new reaction or a new drug may change all our conclusions. Our work has simply established the fact that in certain cases of syphilis of the central nervous system, a definite dosage of one drug will so change the character of the cerebrospinal fluid that it will either give a negative Wassermann reaction or one greatly reduced in positive strength.

We do not suppose that there is any difference in principle, pathologically, between the cases which can be influenced and those which cannot; in certain doses the drug we have employed can reach the site

of the activity of the virus in one case, whilst in the other it is materially ineffective. Our statements are therefore of diagnostic and prognostic value solely under the present conditions of therapeutics and with the serological methods we have employed. We have established what these methods can do, but in no way suggest an essential pathological difference between the two classes. Nor do we believe that any line can be drawn scientifically between the two conditions. Sometimes the virus is acting mainly on the connective tissues and vessels, sometimes on the neuroglia and essential nerve-structures; but in many instances its activity must be widely distributed. At present our power of changing the character of the Wassermann reaction in the cerebrospinal fluid and of materially influencing the disease within a comparatively short period is confined to the cases where the lesion is mainly meningo-vascular. But a new drug, capable of penetrating to the essential structures of the nervous system, may render syphilis centralis amenable to treatment, and our categories will at once cease to have their present value.

The character of the Wassermann reaction in the cerebrospinal fluid can be profoundly influenced in many cases by suitable treatment, and the general condition of the patient may be greatly improved. But whenever syphilis has been active in the central nervous system for any considerable period, the phenomena of which the patient complains still persist to a greater or less extent. This disappointing result is due to the secondary changes which must occur in the structure of the nervous system in consequence of the mechanical effects of the syphilitic lesions. The patient is left with some permanent destruction in almost every case. A man remains characteristically tabetic although the morbid process has apparently died out (No. 83, p. 102). Primary optic atrophy or amyotrophy may remain unchanged although the Wassermann reaction has become negative in both serum and cerebrospinal fluid. In the same way a residual dementia may be left after an attack of so-called "encephalitis" has passed away (No. 59, p. 37). Even gastric crises are not necessarily brought to an end by the apparent cessation of the active syphilitic process (No. 147, p. 22).

When once a portion of the central nervous system, such as the optic nerve or the long tracts in the posterior columns, has been destroyed we should not expect the functions performed by these structures to be restored. The patient remains blind or ataxic. Moreover this research has taught us that paroxysmal manifestations are not

necessarily produced by acute disease. Recurrent pains and paroxysmal vomiting do not necessarily cease because clinical observation and the Wassermann reaction in the cerebrospinal fluid show that the disease is no longer active. Throughout our work we have found many examples of the law, little recognized by neurologists, that a stationary disease may produce paroxysmal manifestations.

If these secondary changes are to be avoided, the diagnosis of cerebrospinal syphilis must be made early in the course of the disease; we must not wait until a man has become spastic or hemiplegic or shows profound muscular wasting before recognizing that the virus is active in his central nervous system. The changes in character and aptitude, the headaches, malaise, attacks of shivering, neurasthenic symptoms and the early manifestations described in Chapter III should at once arouse suspicion that the central nervous system is infected.

But of all the early symptoms changes in sensibility are among the most important; they demand, however, the most careful examination. The ordinary rough methods in unskilled hands are more liable to lead to confusion than to clearness of diagnosis. But when skilfully investigated, the over-reaction to unpleasant stimuli, the slight loss of sensation within areas of apparent hyperalgesia, the bands of changed sensibility, &c., form an important aid to early diagnosis. Moreover, these abnormal sensations disappear rapidly after efficient treatment, and usually leave no permanent disability behind them.

On looking through our records of these root-affections it is at once evident that some areas tend to appear more often than others, and we should like to suggest a possible reason for this fact. According to Orr and Rows [17] the perineural lymphatic space which surrounds every spinal nerve and extends along the roots to the pia mater is an afferent lymphatic channel of the cerebrospinal axis. Toxic material ascends by this system of lymph-spaces from the skin or other deep foci of infection to produce profound changes in the nervous system. On its path inwards through the spinal nerve-roots the poison is liable to produce in them an inflammatory reaction. Both Ehrmann and Levaditi have shown that the *Spirochæta pallida* may pass from a primary sore up the peripheral nerves, and it probably reaches the central nervous system by way of the spinal nerve-roots.

Now we find that the roots most commonly subjected to irritation are those in connexion, by their visceral afferent fibres, with certain organs known to be the seat of active spirochætosis in syphilis. Thus

the second and third cervical, as we know from referred pain, contain the afferent paths from the tonsil. Another common group of root-areas is the first, second, third, and fourth thoracic which contain the afferent paths from the aorta to the central nervous system. But of all the root-areas which appear in syphilis, those from the seventh thoracic to the first lumbar are the most frequent. These roots carry the afferent paths from the liver, kidney, suprarenal and testicle, organs above all others liable to be crowded with spirochætes.

Lastly, we come to the second, third and fourth sacral; the affection of these roots probably has a double origin, and is partly due to the frequency with which secondary syphilitic manifestations appear round the anus. Possibly, however, these roots become infected from the penis and urethra, with which they are intimately connected.

We believe that this infection usually occurs in the secondary period, but dies away rapidly under general treatment. Later, however, it is liable to blaze up again and produce those symptoms and signs of irritation of the posterior nerve-roots which we believe to be of such diagnostic importance.

SUMMARY.

(1) All manifestations of syphilis of the central nervous system are consequent on the direct activity of the *Spirochæta pallida*.

(2) The clinical picture evoked depends on the situation of this activity and on the susceptibility of the tissues.

(3) When the lesion lies mainly within the essential structures of the central nervous system both neuroglia and the nerve elements participate in the tissue-reaction. This results in the death and degeneration of certain systems of cells and fibres; to these secondary consequences may be due the greater part of the clinical manifestations [Chapter V, p. 86].

(4) The more closely clinical signs and symptoms point to pathological changes in the meninges and vessels, the more certainly will the disease yield to adequate treatment [Chapter IV, p. 84].

On the other hand, the more nearly the clinical manifestations point to one or more foci of syphilitic activity within the parenchymatous tissues of the central nervous system, the less will they yield to the present methods of anti-syphilitic treatment [Chapter V, p. 124].

(5) In syphilis meningo-vascularis the character of the Wassermann reaction in the cerebrospinal fluid depends upon whether the spinal or

basal meninges are affected. Should clinical evidence point to affection of the contents of the spinal canal, and occasionally when the basal meninges alone appear to be affected, the reaction is positive in the cerebrospinal fluid. When, however, the disease seems to be limited to the intracranial contents, the reaction in the cerebrospinal fluid tends to be negative or weakly positive [Chapter IV, p. 79].

(6) In cases of syphilis centralis, such as dementia paralytica, tabes dorsalis, muscular atrophy and primary optic atrophy, the Wassermann reaction in the cerebrospinal fluid is strongly positive so long as the disease is active. When, however, it has come to an end, leaving behind it a greater or less amount of irreparable degeneration, the Wassermann reaction may diminish in strength or even become negative in the cerebrospinal fluid [Chapter V, p. 101].

(7) Under treatment with salvarsan or neosalvarsan, the Wassermann reaction in cases of meningo-vascular syphilis, if at first positive, will usually become negative in the cerebrospinal fluid within six months [Chapter IV, p. 84].

On the other hand, the more the clinical manifestations point to syphilis centralis the less will they yield to any of the present forms of anti-syphilitic treatment [Chapter V, p. 124, and Chapter VI, p. 126].

(8) Thus no complete diagnosis or prognosis can be made until the patient has been under observation and treatment for at least six months, and the cerebrospinal fluid has been systematically examined from time to time.

(9) It is essential to employ a standard serological technique, such that the Wassermann reaction can be estimated quantitatively. The results given in this paper bear testimony to the uniformity and trustworthiness of the methods adopted by Dr. Fildes for performing the Wassermann reaction (Fildes and McIntosh [3]).

(10) Whatever the situation and nature of the lesion which is responsible for the clinical manifestations, some secondary degeneration must almost certainly result. Many of the signs and symptoms in cases of syphilitic disease of the central nervous system are therefore not amenable to any form of anti-syphilitic treatment.

(11) It is, therefore, most important to make the diagnosis of syphilis early in disease of the central nervous system, so that treatment may be employed before the advent of these secondary changes. In Chapter III we have considered a number of nervous conditions which are early manifestations of syphilitic disease (p. 7).

REFERENCES.

- [1] DEJERINE. *Rev. de Méd.*, 1889, t. ix, pp. 81 and 208.
- [2] DONALD. *Folia Hæmatologica*, 1913, Bd. xvii, S. 139.
- [3] FILDES and McINTOSH. *Brain*, 1913, vol. xxxvi, p. 193.
- [4] FOURNIER. "Les Affections Parasyphilitiques," Paris, 1894.
- [5] HEAD and SHERREN. *Brain*, 1905, vol. xxviii, p. 194.
- [6] HEUBNER. Ziemssen's "Handbuch d. sp. Path. u. Therap.," Leipzig, 1876, Bd. xi, S. 277.
- [7] LÉRI. Congrès des Aliénistes et Neurologistes, Bruxelles, 1903. [Reported in *Revue Neurologique*, 1903, t. xi, p. 849.]
- [8] *Idem*. XVII Internat. Congress of Med., 1913, Section XI, Neuropathology, part ii, p. 261.
- [9] LÉRI et LEROUGE. *Gazette des Hôpitaux*, 17 mai 1913, 86 année, p. 885.
- [10] McINTOSH, FILDES, HEAD and FEARNSIDES. *Brain*, 1913, vol. xxxvi, p. 1.
- [11] MOTT. XVII Internat. Congress of Med., 1913, Section XI, Neuropathology, part p. 259.
- [12] *Idem*. *Arch. of Neurol. and Psychiat.*, London, 1914, vol. vi, p. 1.
- [13] NONNE. "Syphilis u. Nervensystem," Zweite Auflage, Berlin, 1909.
- [14] *Idem*. XVII Internat. Congress of Med., 1913, Section XI, part ii, p. 300.
- [15] *Idem*. *Deutsch. Zeitschr. f. Nervenheilk.*, 1914, Bd. li, S. 155.
- [16] OPPENHEIM. "Die Syphilitischen Erkrankungen des Gehirns," *Nothnagel's Handbuch*, Wien, 1896, Bd. ix.
- [17] ORR and ROWS. *Brain*, 1914, vol. xxxvi, p. 271. [This paper contains references to the other communications of these authors on the same subject.]
- [18] PLAUT. "Ueber Halluzinosen der Syphilitiker," Berlin, 1913.
- [19] PLAUT, REHM und SCHOTTMÜLLER. "Leitfaden zur Untersuchung der Zerebrospinalflüssigkeit," Jena, 1913, S. 28.
- [20] RAYMOND. *Bull. et Mém. de la Soc. Méd. des Hôp. de Paris*, fév. 3, 1893, t. x, p. 55.
- [21] SWIFT and ELLIS. *New York Med. Journ.*, 1912, vol. xcvi, p. 53.
- [22] UHTHOFF. "Ueber d. bei d. Syphilis d. Centralnervensystems vorkommenden Augenstörungen," Leipzig, 1894, S. 306.

A COMPARISON OF THE LESIONS OF SYPHILIS AND "PARASYPHILIS," TOGETHER WITH EVIDENCE IN FAVOUR OF THE IDENTITY OF THESE TWO CONDITIONS.

BY JAMES McINTOSH, M.D.ABERD.

Beit Memorial Research Fellow ; Late Research Scholar of the Grocers' Company

AND

PAUL FILDES, M.B., B.C.CANTAB.

Assistant Bacteriologist to the London Hospital.

From the Bacteriological Laboratory of the London Hospital.

(Professor William Bulloch, F.R.S.)

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In a previous paper [22] we have published a short review of the evolution of opinion regarding the relation of "parasyphilis" to syphilis of the nervous system.

Originally, syphilis was not even considered to be an essential precursor of "parasyphilis," but gradually it became evident that without syphilis there was no "parasyphilis." This latter condition was looked upon as a non-syphilitic sequel of syphilis; a form of degeneration consequent upon syphilis, but not an active syphilitic inflammation due to the virus of the disease. On the other hand, more recently the opinion has been repeatedly expressed that "parasyphilis" is an active inflammatory process presumably due to the *Spirochæta pallida*, but differing from the ordinary manifestations of syphilis in some unknown particular. On the whole very little attention has been paid to such suggestions, since little effort was made to account for the admitted distinctions between syphilis and "parasyphilis" of the nervous system.

For the past three years, in collaboration with Dr. Head and Dr. Fearnside, we have been engaged in a study of these questions, and our general conclusions have been shortly summarized already [23].

We expressed the view that "parasyphilitic" diseases are essentially syphilitic; that they are not degenerative sequelæ of syphilis, but are themselves active syphilitic processes due to the *Spirochæta pallida*; finally, that they are not syphilitic lesions of an unusual or particular form, but that they resemble in all essentials such lesions found elsewhere in the body.

In order to elaborate this view, we analyse in the following pages the exact type and nature of syphilitic lesions throughout the body generally, and then compare them with the essential lesions of "parasyphilis."

This paper is intended to be read in conjunction with our publication upon the Wassermann reaction [7], and also with that by Dr. Head and Dr. Fearnside appearing in the present issue.

We desire to express our thanks to Professor Bulloch again for the continued interest he has taken in our work.

CHAPTER I.—THE TISSUE REACTION IN SYPHILIS.

INTRODUCTION.

The variety of the lesions occurring in the course of syphilis, and the definite progression of the different stages are phenomena which have been well recognized since the earliest times.

It was known that the infection gave rise to a local sore, that the local sore was soon followed by a general exanthem, and finally, that

after a lapse of time sequelæ of a distinctive type might follow. The disease thus came to be divided into three periods often called "the period of local eruption," "the period of general eruption," and the "period of gummy deposits."

This classification has dominated the pathology of syphilis until the present day. The three periods were taken to represent definite stages in the progress of the disease, the local and general eruption and the gummy deposit being the characteristic features of these periods. In the period of local eruption the virus was thought to be entirely localized, while the general eruption marked the time of generalization. The gummy deposit, on the other hand, was looked upon as an entirely different type of lesion to those found in the first two stages, and, in fact, its dependence upon the virus of syphilis was often disputed.

In this manner has arisen the belief that the chancre, the cutaneous rash and the gumma are the characteristic manifestations of the three stages of syphilis, and that being characteristic they are capable of being readily distinguished one from another by pathological or clinical methods.

On investigation, however, it will be found that these lesions can only be described as "characteristic" in general terms. The primary sore, indeed, presents features very different from the lesions of the secondary stage, and similarly these latter may be readily differentiated from "tertiary" granulomata; but nevertheless it must be remembered that the macroscopic features by which these various lesions are recognized are frequently ill-developed, and it may then be difficult to determine the exact stages to which they belong.

An ulceration of the penis may be so "atypical" that the question may be debated as to whether it is a "primary sore" or a tertiary "pseudo-chancre," and similarly some of the cutaneous ulcerations of late secondary syphilis have so little in common with an ordinary secondary lesion that they may be looked upon as tertiary. Thus, although it may be admitted that the manifestations of syphilis in their most typical forms are characteristic for the various stages of the disease, nevertheless there is no definite particular in which one stage may be said to differ essentially from another.

Even in the microscopic anatomy the differentiation is no more precisely marked; it is often said that the occurrence of "endarteritis" or even a peculiar liability to necrosis is a feature of tertiary syphilis, but on critical analysis it is found that both "endarteritis" and necrosis are familiar features of all stages and are not characteristic only of the

tertiary period. They are merely present at this time in their most pronounced form. In fact, if in early examples the essentials of syphilitic lesions are studied, it will be found that they exhibit a general similarity, and that, as Virchow first pointed out, the appearances "characteristic" of the various stages are due to entirely secondary phenomena.

THE COMPARATIVE HISTOLOGY OF THE SO-CALLED "CHARACTERISTIC" LESIONS OF SYPHILIS.

If the histology of a primary sore be examined it is found to consist of a granuloma, the most marked features of which are perivascular collections of lymphocytes and plasma-cells, associated with a proliferation of the walls of the affected vessels. This proliferation may, indeed, lead to obliteration and thrombosis as a secondary phenomenon, and later an overgrowth of the connective tissue may produce a general fibrosis.

The cutaneous lesions of the secondary period are essentially similar and differ only in their greater acuteness. The capillaries are congested and their walls are proliferated, while surrounding the vessels are collections of lymphocytes and plasma-cells. In the more chronic affections an induration may be produced, as in the primary sore, by the overgrowth of fibroblasts.

Again, the tertiary lesion, the gumma, in favourable specimens may be observed to have its origin in a perivascular inflammation. The same proliferation of the vessel wall is manifest and the same accumulation of cells. The chief difference lies in the more pronounced secondary effects of the process. The cell accumulations are larger and more focal and the proliferation of the fibroblasts more marked. Thus the interruption in the blood supply and other factors determine an early degeneration and more marked necrosis in these foci.

The distribution of the *Spirochæta pallida* in these lesions is also very similar.

In the primary sore they are found in large numbers among the cells of the Malpighian layer and in the subcutaneous lymphatics. Further they are associated with the perivascular accumulations of cells, in the walls and actually in the lumen of the affected vessels. The same distribution occurs in the secondary lesion, although in this case the organisms are particularly concentrated upon the walls of the vessels rather than in the surrounding lymphatics.

In the gumma the relation of the spirochætes to the cellular histology is less well known, since in these lesions they are extremely

sparse. From an examination of the miliary gummata as found in the liver of a congenital syphilitic foetus, it is seen that the organisms are in the proliferated walls of the central vessel and a similar relation has been described in very early gummatous lesions of the adult. In most cases of acquired tertiary syphilis, however, the degenerative process is already so far advanced before the lesion comes under observation that spirochætes can seldom be demonstrated. Indeed it has been supposed by some that the virus is not present in such cases in the form of a spirochæte, but such suggestions are negatived by several well authenticated instances. It is undoubtedly true that very few organisms are found in tertiary lesions, as might be supposed from their trivial infectivity, and this fact constitutes one of the most striking differences between early and late syphilis. In the former, the lesions of the acute stage, the spirochætes are numerous; in the latter, the chronic manifestations, they are few in number.

From the foregoing account it will be seen that as regards the histology of the "characteristic" lesions there is no essential difference in the three stages. They all contain the *Spirochæta pallida*, and this organism represents the irritant about which the cell reaction is found. Nevertheless, the tertiary process undoubtedly differs from the primary and secondary in that it is caused by a very much smaller number of spirochætes. This difference may be looked upon as a qualitative difference, and the same may be observed in the cellular reactions. In all cases the lesion is found to consist of an infiltration of lymphocytes, plasma-cells, and, usually, fibroblasts. There is a great tendency to form accumulations in relation to blood-vessels and these accumulations are swollen by a proliferation of the actual walls of the vessels themselves.

Such differences as are found between the appearance of the lesions of syphilis in the mesoblastic tissues depend chiefly upon the acuteness or chronicity of the condition. The type of the constituent cells is the same, but the different varieties are present in different proportions and undergo different modes of resolution or degeneration.

THE COMPARATIVE PATHOLOGY OF SYPHILITIC LESIONS.

In the preceding section we have shown that the "characteristic" cell reaction to the *Spirochæta pallida* is very similar in both acute and chronic syphilis. It is, however, necessary to point out that we have only dealt with those cell reactions which have for long monopolized

attention, namely, the reactions of the mesoblastic tissues. The disease of syphilis is too often studied as a series of cutaneous manifestations. There is a tendency to look upon the secondary period as the period of the rash, or upon the tertiary as the period of ulceration of the skin. It must not be forgotten that syphilis is not a disease of the skin; it is a general infection which involves all parts of the body at all periods. The skin lesions are only remarkable in that they are the most obvious. Their importance is certainly secondary to the affections of the internal organs.

We will therefore compare the pathology of the "characteristic" lesions already described with that of the internal organs.

For this purpose it is only necessary to discuss two periods of syphilis; the acute, corresponding to the secondary, and the chronic or tertiary.

The term "primary period" is strictly a misnomer. There is no primary period from the pathological point of view. A lesion, indeed, usually occurs at the point of inoculation, but this lesion is merely an incident in the incubation period of the acute symptoms. Its occurrence is more or less accidental and, as is now well known, it is often absent.

It will be remembered that within a few hours after inoculation the spirochaetes have already wandered into the regional lymphatics and that within a few days they may be detected in the blood and internal organs. The virus is therefore generalized long before the appearance of the primary sore and this lesion cannot be looked upon as denoting a "period of local eruption." Conveyed by the blood-stream the spirochaetes may lodge in any internal organ, spreading through the capillary walls and wandering through the lymphatics into the essential parenchyma itself.

This invasion of the internal organs in the acute stage leads sometimes to symptoms of great gravity, but for the most part the effect is not severe. An invasion of the liver may cause jaundice, or a nephritis or orchitis may occur; on the other hand the intoxication of the organ may be excessive and lead to widespread destruction of the parenchyma. This effect upon the organs is not merely due to the effect of the virus upon the interstitial tissues, such as may be seen in the cutaneous lesions, giving rise to a perivascular proliferation and infiltration of small cells; it is due chiefly to a primary intoxication of the parenchyma itself.

The effect of the intoxication upon the two types of tissue, interstitial and parenchymatous, will apparently be different, although essentially

of the same nature. There will be a reaction to stimulus, and in this reaction some of the cells will succumb and degenerate. The difference between the interstitial tissues and the parenchyma is that in the former the reaction is marked—proliferation and infiltration—while the degeneration is slight, and in the latter the reaction is trivial and the degeneration extensive.

This result is due to the different functions of the two types of tissue. One of the activities of the interstitial tissue is to proliferate and combat, in a phagocytic sense, a microbic infection. The parenchyma, on the other hand, is devoted to some particular metabolic function; it is a specialized tissue which does not participate in a phagocytic reaction. It has only a limited power of repair or regeneration, and therefore if the intoxication exceeds a certain limit, degeneration will follow.

In this manner in the acute stage of syphilis lesions of the internal organs may occur, in which a varying degree of degeneration of the parenchyma is found. The extent of the destruction depends upon the extent to which the spirochætes migrate from the capillaries and lymph spaces.

As the acute stage of syphilis subsides, there is a general destruction of the spirochætes throughout the body, but as shown by the subsequent relapses the destruction is not complete. Isolated foci are left in those organs and parts of the body into which the destructive agents, whether drugs or natural antibodies, have not succeeded in penetrating. In these situations the spirochætes lie "dormant," but are capable of exacerbation, under circumstances which are not understood, and of producing tertiary lesions.

The "typical" tertiary lesion, as already described, is the gumma, but just as a papule is not the only secondary lesion, so the gumma is not the only result of the exacerbation of the *Spirochæta pallida*. A gumma is produced by a focus occurring in or about the wall of a small blood-vessel; it is a perivascular proliferation and infiltration of the interstitial tissues, and when occurring in an organ, the intoxication only affects the parenchyma in the immediate neighbourhood of the focal lesion. In tertiary syphilis, however, there are types of organ lesions which are sometimes referred to as "non-gummatous" or as diffuse infiltrations, leading to a diffuse fibrosis and destruction of the parenchyma. This type of lesion is comparable to the diffuse inflammations of the acute period. The intoxication is not focal as in the gumma, but diffuse, and, therefore, there is not only a diffuse reaction of the interstitial

tissues but a diffuse intoxication and resultant degeneration of the parenchyma.

It may be said, therefore, that the lesions of syphilis are similar both in the acute and chronic stages; in each the interstitial tissues and the parenchymatous tissues are involved. The affections are of two main types; the focal represented by the papule and the gumma, in which the virus is perivascular and exerts its effect chiefly upon the interstitial tissues; and the diffuse, in which the intoxication is diffuse and in which the effect, therefore, falls most obviously upon the parenchyma.

The ultimate result of these two varieties of lesion upon the integrity of the organ will be entirely different. The interstitial lesion need produce no notable symptoms and derange no important function; with suitable treatment it may entirely resolve. It is, however, quite different in the case of the parenchymatous lesions. As already described, if the intoxication proceeds beyond the narrow limit of repair, the cells will degenerate, and with them will be lost the special function of the organ. Under these circumstances the treatment, which was efficient in dealing with the interstitial lesion, will be without avail. The symptoms will be occasioned not by the presence of syphilis, but by the absence of the parenchymatous tissue. This loss of function, well illustrated by the sterility following a parenchymatous orchitis, is irreparable.

Syphilitic lesions of the liver.—The pathology of the lesions produced by syphilis in the internal organs may be illustrated by a consideration of the affections of the liver.

In this organ the extreme types of syphilitic inflammation are to be found in the "acute yellow atrophy" and the "solitary gumma." Both these conditions may be described as rare. The former has been recorded as occurring in the early secondary stage and is due to a diffuse dissemination of the virus throughout the organ. Microscopically, there is found a profound general degeneration of the liver-cells with little, if any, interstitial reaction, at most an infiltration of lymphocytes. The disease runs a rapid course and ends in death.

The gumma of the liver, on the other hand, is a purely local lesion, and originates in a reaction about a focus of spirochaetes lying around a blood-vessel. The virus will produce about itself a reaction both of the parenchyma and also of the interstitial tissues, but since the destruction of the former will be purely local the result will not obtrude itself upon the microscopic picture. The interstitial reaction,

on the other hand, will consist of a local proliferation of the fixed cells and an accumulation of the wandering cells, and this focal reaction will result in a conspicuous granuloma. The liver-cells surrounding the focus will be separated by the infiltrating wandering cells, but this infiltration does not necessarily imply the presence of the spirochætes in its midst. The cells merely utilize the lymphatic spaces as channels by which to reach the virus, situated in the main focus of attraction. The tissues in which they lie are not directly affected by the spirochæte any more than the blood is affected in leucocytosis by the cocci in an abscess. Thus the main mass of liver-tissue proper surrounding a gummatous focus is more or less normal; only those cells in the immediate vicinity of the initial focus are destroyed.

In acute yellow atrophy, therefore, since the distribution of the virus is diffuse, the reaction and destruction is most marked in the parenchyma, while in the focal gumma the most obvious effect is upon the interstitial tissues.

The two extremes mentioned are, however, rare, and many intermediate types are found. The gummatous process, for instance, usually results from the fusion of a number of smaller foci and according as the virus is more or less diffused from these foci, the parenchyma is more or less involved in the process. Thus a diffuse reaction in the parenchyma may be associated with focal gumma formation in the same liver.

Certain examples of congenital syphilitic livers illustrate the mean between the two extreme types. In these cases the invasion from the portal vein results in a very large number of points of infection. The spirochætes lodge in the small vessels and multiply in their walls. From here they invade the surrounding lymphatics and even the liver-cells themselves. As a result a general reaction will take place both of the parenchyma and also of the interstitial tissues. The parenchymatous reaction is evidenced by duplication of the nuclei, and cell masses may be observed containing multiple nuclei and karyokinetic figures. This reaction of the parenchyma will usually end in a diffuse degeneration. The interstitial reaction is most marked about the infected vessels, and consists of an endothelial proliferation, while wandering lymphocytes fill the lymphatics between the liver-cells. The larger collections of cells tend to degenerate and form miliary gummata, while the more diffuse interstitial reaction leads to a diffused fibrosis of the organ. In such a case the incidence of the virus upon the two main types of tissues is relatively equal.

CONCLUSIONS.

(1) The interstitial lesions of syphilis should not be looked upon as "characteristic" of syphilis to the exclusion of the parenchymatous. In addition to the interstitial reactions in the skin and internal organs, the essential parenchyma of these organs is also primarily involved in the intoxication.

(2) As a result of the stimulation by the virus the interstitial tissues will undergo a proliferation, but this will be absent or abortive in the case of the parenchyma. This tissue will usually degenerate, being incapable of extensive repair, and the secondary degeneration will entail a loss of function which will be unaffected by anti-syphilitic treatment.

(3) The above result is the effect of a diffuse dissemination of the virus, but if the spirochætes appear in a series of foci, the whole process will tend to take on a focal arrangement, and in this case the nodular interstitial reaction will tend to overshadow the local parenchymatous reaction.

CHAPTER II.—THE FACTORS GOVERNING THE AMOUNT OF TISSUE REACTION IN SYPHILIS.

INTRODUCTION.

In the preceding chapter we have shown that syphilis is a disease which affects not only the interstitial tissues at all periods but also the parenchyma of the internal organs and that the essential type of tissue reaction is the same at all stages of the disease. The difference between the appearances of a secondary and tertiary lesion, for instance, is due to secondary changes in the latter. These changes consist of excessive fibrosis and liability to degeneration. Further, we have shown that the number of spirochætes is large in a secondary lesion but small in a tertiary, and it thus follows that in these latter cases there is a remarkable lack of correlation between the amount of the virus and the extent of the lesion. In the secondary stage it requires a large number of spirochætes to produce a papule, while in the tertiary stage a large gumma may result from a number of spirochætes which is too small to detect. It therefore becomes necessary to inquire into the factors which govern the extent to which the tissues may react to the virus.

THEORIES ON THE RELATION OF THE VIRUS TO THE LESION.

At the present time every syphilitic lesion is looked upon as a response to the stimulus of the *Spirochæta pallida*. In former years, however, it was generally held that the tertiary lesions were not the direct effect of the virus and this view was supported by their notoriously slight infectivity. The discussion of the nature of the gummatous process was opened by Sir Jonathan Hutchinson [15] in 1866 as follows: "The occurrence of the tertiary symptoms is to be explained by the fact that during the exanthematic stage, when the whole blood was loaded with the virus, the various solids have received from that poisoned blood the elements necessary for their growth, and have been built up, so to speak, with syphilized plasma. Hence an impairment of organization in such tissues, and a liability under slight exciting causes . . . to the occurrence of specific forms of inflammation." Again, "The tertiary symptoms are not so properly a stage, but must count rather as the sequelæ, more or less accidental, of the preceding stages. They are as a rule not symmetrical, making it seem improbable that they depend upon blood taint. . . . From these facts we infer that they are due rather to the ill constitution of the affected structures than to any free virus still circulating in the blood."

It will be seen from the above quotations that the gumma was not looked upon as a syphilitic lesion in the sense that it was due directly to the virus of syphilis. Hutchinson considered that the syphilitic infection produced a state of body or diathesis in some ways akin to the scrofulous diathesis. This condition of the tissues ensured that any stimulus applied to them would produce the type of reaction known as a gumma.

In 1874 Bäumlér [2] expressed very similar views. He looked upon the primary and secondary manifestations as the direct irritant result of the syphilitic virus affecting normal tissues, but "during the period of gummatous development it is probably no longer the action of the specific poison upon normal tissue with which we have to do, but with a sort of specific reaction of tissues, modified by previous blood-poisoning, under some accidental irritation."

Here, again, the gumma is looked upon as a specific lesion due to a non-specific cause, the specificity of the reaction being due to an alteration in the tissues induced by the previous infection.

So far as we are aware the first true recognition of the relation of the virus to the tertiary lesion is due to Eduard Lang [18]. In 1881 he stated that the virus of syphilis became disseminated throughout

the organs of the body at the time of the exanthem, but that subsequently the greater part was destroyed, "a remnant only lies latent in the tissues and this becomes manifest after any injury through the local production of new growths which are occasioned by the exacerbation of the virus, now essentially altered in character. The new growths represent the late forms of syphilis."

Lang further laid down the rule that "an organ which is the seat of a gummatous lesion must have been affected in the early period of syphilis."

It is thus clear that Lang differed from Hutchinson and the other syphilologists of the time in ascribing the tertiary lesion to the direct action of the virus, while the alteration in the appearance of these lesions was considered to be due to an alteration in the virus rather than in the tissues themselves.

Almost simultaneously Neisser [29] (1882) recognized the essential dependence of the gumma upon the activity of the virus. He, however, reverted to the theory of tissue alteration to account for the characters of the tertiary lesion, and referred to this alteration as an "Umstimmung der Gewebe," resulting from the action of the virus during the secondary period.

"This alteration in the tissues, soon after the infection, as soon as the disease has become constitutional, becomes an additional factor which has to be taken into account whenever the action of the virus itself is discussed. It certainly has nothing to do with a so-called anomaly of constitution (scrofulous, scorbutic, &c.), but is a specific alteration which the tissues undergo when they are themselves bathed in syphilis toxin."

Neisser was thus the first to look upon the tertiary process as an expression of the activity of the virus exerted upon tissues which had undergone a specific alteration after the acute period.

There can be but little doubt that the theory of tissue alteration propounded by Neisser, as opposed to the alteration in the virus suggested by Lang, is the correct explanation. It has been, however, frequently suggested that the different types of lesion associated with syphilis may be due to alterations in the virulence of the spirochæte, but while the possibility of such altered virulence must not be lost sight of, this view must be held to lack sufficient support.

When normal animals are inoculated with tertiary material, the resultant lesion is a typical primary sore with a relatively normal incubation period, and the primary lesion in the chimpanzee is

followed by a normal secondary stage. In some cases the incubation period is found to be prolonged, and this has been taken as evidence that the virus in tertiary syphilis is modified or attenuated. This may, indeed, be the case, but at the same time the prolonged incubation period may merely result from the small number of spirochætes in the inoculated material. A "tertiary" spirochæte, then, does not produce a "tertiary" lesion in a non-syphilitic individual, but a "primary" spirochæte will produce a "tertiary" lesion in a "tertiary" syphilitic (indurated pseudo-chancere, *vide* p. 155).

It is therefore clear that variation of the spirochæte has little bearing upon the differences in the appearance of syphilitic lesions at different stages. This is due to an alteration in the tissues produced by the previous activity of the infective agent.

ALLERGIE.

The nature of the alteration in the tissues was not further discussed until von Pirquet introduced his theory of "allergie" (1903).

This term "allergie" was not introduced in connection with syphilis, although von Pirquet [43] considered that this disease would afford a fruitful field for its study. The word was used to denote the alteration in the reactions produced by *second injections* of certain viruses. The original state studied was the "serum disease" produced in man by injections of horse serum, and later he studied vaccination and revaccination in the same light.

The alteration in the reaction following a second inoculation of a virus might be recognized in three ways: Firstly, by an alteration in the reaction *time*; secondly, by an alteration in the *extent* of the reaction; and, thirdly, by an alteration in its *quality*.

A classical example of allergie is found in Jennerian vaccination and revaccination.

Thus, where an individual is vaccinated for the first time, the full development of the pustule is observed on about the twelfth day; when, however, he has already been vaccinated a few months previously, and is then revaccinated, the lesion will attain its full development on the first day (alteration in the reaction time), but the characteristic features of the normal pustule will not develop (alteration in the reaction type), and the whole reaction will be smaller (alteration in the reaction extent).

The alterations in the reaction time are of two main types. Firstly, the immediate reaction ("sofortige Reaktion"), which is met

with when the "immunity" induced by the first injection is still present, and the quickened reaction ("beschleunigte Reaktion") occurring when several years have elapsed since the first injection and the "immune bodies" have disappeared from the serum. In revaccination the immediate reaction is observed when the second inoculation is carried out within about two years of the first; while the quickened reaction, i.e., a relative normal pustule with a shortened incubation period, occurs as a result of revaccination after a longer period.

The manifestation of allergie which most concerns the present subject is, however, the quantitative and qualitative alterations in the cell reaction. The lesion following a second inoculation may be smaller or larger than the primary lesion; in the former case the susceptibility of the tissues to the poison is depressed, and in the latter it is exalted. A well-known example of the latter state is von Pirquet's skin reaction in tuberculosis, when owing to the altered (hypersusceptible) state of the tissues induced by tuberculosis, an inoculation of a minute quantity of tuberculin will produce a large inflammatory lesion. The quality of the reaction will also differ from a primary tuberculous lesion, while the incubation period will be shortened to twenty-four hours.

Von Pirquet suggested that in all probability the manifold varieties of syphilitic lesions were also due to the state of allergie induced by the previous presence of the virus, and pointed out that Finger and Landsteiner had demonstrated a shortened incubation period after second inoculations of syphilitic material in monkeys, while inoculations in tertiary syphilitics produced an immediate ("sofortige") toxic erythema. This lesion he regarded as being due to a hypersusceptible state of the tissues produced originally by the *Spirochæta pallida* and as entirely analogous to the cutaneous reaction in tuberculosis. This view has more recently been accepted by Neisser [30], who stated that his "Umstimmung der Gewebe" was intended to imply an idea exactly similar to von Pirquet's allergie.

ALLERGIE IN SYPHILIS.

In the following pages we enumerate various phenomena which occur in syphilis to illustrate the existence of allergie in this disease.

Syphilization.—Phenomena analogous to those following Jennerian vaccination may be observed in experimental syphilization, the two instances, however, differing, in that the former is a transient infection while the latter is chronic and persistent. As a result of a large number

of experiments on monkeys it has been demonstrated that second inoculations when carried out within a short period of the first (fifty-one days—Neisser) produce a second "primary lesion" with a shortened incubation period. This is a case of "Beschleunigung der Reaktion" due to an increased susceptibility of the tissues resulting from the first inoculation.

The tissues have become altered in such a way that they respond more readily to the stimulus of the virus. Similar results have been obtained by Pinard [42] on man. When, however, the reinoculation with syphilis is attempted in the secondary period, it is found that the virus is practically without effect. Very few instances have been recorded of lesions appearing as a result of reinoculation at this period, and it was only by the method of tissue implantation that Finger and Landsteiner, and Pinard succeeded in producing an insignificant papule. It is thus clear that in the secondary stage the tissues are very little susceptible to the *Spirochæta pallida*, although many of these organisms may have been present in the inoculated material. A change has taken place (allergie) in the direction of diminished susceptibility.

In the tertiary stage, however, the effect of reinoculation with syphilis is quite different. A lesion is produced after a very short incubation period, the so-called "sofortige Reaktion." The area involved is often of considerable size, and tissue destruction is so marked as to lead sometimes to ulceration. The effect of the inoculation is thus to produce a lesion of a "tertiary" character. This extensive reaction is not due to an excessive local growth of the spirochætes, since on examination these are seldom to be found; if they are discovered occasionally they are probably only the remnant of those injected.

Such a reaction is clearly comparable to the tuberculin reaction in tuberculosis. It is an abnormally great reaction of the tissues to the virus. The tissues have again undergone a change (allergie), but in this case in the direction of increased susceptibility. They have become hypersusceptible and, therefore, react in an excessive manner out of all proportion to the quantity of spirochætes injected.

Syphilization in tertiary syphilis is commonly observed as the "indurated pseudo-chancere." This is an ulcerative lesion of a "tertiary" character and very seldom contains the *Spirochæta pallida*. It is without doubt produced by the implantation of a new strain of spirochætes upon a tertiary syphilitic. Instead of a Hunterian chancre appearing after a long incubation period, the hypersusceptible tissues react quickly as a tertiary lesion. These lesions are not "chancres"

and should not be described as "reinfections." They are super-infections and their appearance is due to an alteration in the tissues; the inoculated spirochætes do not multiply and they produce no constitutional symptoms.

Cutaneous reactions.—Results very similar to those obtained by syphilization may follow the application of the luetin test of Noguchi [32 and 33]. This test consists of the percutaneous injection of dead *Spirochæta pallidæ* obtained from cultures and is thus directly comparable to the cutaneous test of von Pirquet in tuberculosis. As a measure of allergie this test is less complex than is syphilization, since the effect is not obscured by the production or absence of the disease syphilis as a result of the inoculation.

We have found that in the later primary stage a slight positive reaction may usually be obtained, demonstrating an increased susceptibility in the tissues. During the secondary period, however, no effect is produced, since the tissues are not susceptible. In the tertiary period, on the other hand, the positive reaction is often very marked as a widespread inflammatory lesion. In non-syphilitic persons the inoculation produces no effect, although it must be admitted that as a diagnostic measure the test cannot be looked upon as being specific. By this method, therefore, it may be seen that a quantity of dead virus, which in itself is non-toxic, is capable of producing a lesion in syphilis at certain periods, these periods being marked by a condition of increased susceptibility to this virus. If in normal tissues a certain quantity of virus is capable of producing no effect, in hypersusceptible tissues the same quantity may produce a great effect.

Allergie observed during the progress of the syphilitic infection.—In the previous sections, we have described the state of allergie in the various stages of syphilis as demonstrated by reinoculations of syphilitic material, but a similar phenomenon may be observed in the actual manifestations of the disease.

Syphilis should be looked upon as exhibiting two periods only, namely, the acute, corresponding to the secondary, and the chronic or tertiary. For the purposes of simplification the primary stage so called may be omitted, since in fact it is merely an incident in the incubation period of the acute symptoms.

Both the acute and chronic lesions are reactions against a local toxin derived from the *Spirochæta pallida*, and the variable type of reaction (allergie) depends upon the different states of the tissues induced by this organism. At the time of infection the tissues are prac-

tically insusceptible to the *Spirochæta pallida*, and therefore no immediate reaction occurs. The local growth and rapid generalization of the virus, however, produces such an effect upon the tissues that they become more susceptible and thus develop an immunity reaction against the virus. This reaction is both "cellular" and "humoral," that is to say the tissues not only become more prone to a cellular reaction but also produce antibodies. The period of time which elapses before the immunity response has developed corresponds to the incubation period of the acute manifestations. The production of antibodies in protozoal diseases is often "critical," and thus in syphilis a "critical" output of antibodies occurs and leads to a "critical" destruction of a large number of spirochætes, and the consequent liberation of large quantities of toxins. These toxins will affect the sensitized tissues and create a generalized reaction or acute rash. The exanthem may thus be looked upon as representing a reaction to a dose of syphilis toxin in tissues which have undergone a certain degree of sensitization. These are more susceptible to the virus than they were before infection took place.

Following the rash, however, as has already been shown, the tissues have lost their susceptibility in that at this time an inoculation of the virus will produce practically no effect. This result is probably due to the phenomenon of "desensitization." It is known that when an animal has been rendered hypersusceptible to serum, for instance, this hypersusceptibility may be abolished under certain conditions by the reintroduction of the antigen (serum). Similarly the susceptible cells in syphilis may be rendered insusceptible by the general liberation of antigen (spirochæte toxin) at the time of the secondary rash. In the phraseology of Ehrlich it may be said that the avidity of the cell receptors is entirely satisfied by the virus and no excess of avidity (susceptibility) is left.

In this condition the cells in the manner of von Pirquet may be described as being "anergic," and it is in consequence of this anergie that the manifestations gradually disappear after the period of the exanthem.

During the "latent period," the virus is still retained in the body, producing an effect, outwardly at least, inappreciable, or in an entirely dormant state. At this time an increased susceptibility gradually develops in the tissues. The degree of susceptibility is much greater than that present in the early stage of the disease and thus, on exacerbation of the spirochætes, a lesion will be produced which is larger than a "secondary" tissue reaction, and which will show an alteration

in type leading to excessive degenerative changes (hyperallergie, hypersusceptibility). The alteration in the incubation period, on which great stress is laid by von Pirquet, cannot be demonstrated in the spontaneous tertiary lesion, since the actual time of exacerbation cannot be determined. In those cases, however, in which the tertiary lesion is produced by a foreign strain, that is, when an "indurated pseudo-chancere" follows from a superinfection in a tertiary syphilitic, it may be observed clearly that the incubation period is very much shortened, being reduced from one month, as in the primary period, to at most a few days ("Beschleunigung der Reaktion").

The alteration in the reaction of the tissues (allergie) is particularly obvious when attention is paid to the actual number of spirochætes giving rise to the various lesions. In the secondary stage, although the reaction is less, the number of spirochætes in the lesions is large, while in the tertiary lesions, even when of large size, the number of spirochætes is small; in fact in practice it is extremely difficult to demonstrate them in such lesions.

The reaction of the tissues in chronic syphilis has not only undergone a change in its extent, but the character of the cells is also different. As has already been pointed out, the initial lesion is the same in all forms of syphilis, but in chronic syphilis the secondary changes tend toward fibrosis and degeneration. This excessive degeneration is due to the hypersusceptibility of the cells. Although the hypersusceptible state is an immunity process designed as a protective mechanism by which the whole of the antimicrobial forces are rapidly brought into play, nevertheless the increased avidity of the cell receptors leads to an intoxication of the cells which is often excessive. Thus the tissues are not only more easily thrown into activity but are also more readily injured. The degeneration consequent upon this injury is the cause of the most "characteristic" features of tertiary syphilis, namely, the necrosis of gummatous tissue.

So long as the degeneration is confined to the interstitial tissues, the site of a gumma, no serious incapacitation of the patient need follow, but when a vital organ, and particularly the parenchyma of such an organ, is involved, the result is more important. If these cells have been rendered hypersusceptible and are then exposed to the action of the virus, they will usually be intoxicated beyond the limit of repair and will undergo a progressive degeneration which will entail a complete and irreparable loss of function of the organ.

The factors which determine the occurrence of the hyperallergic

reaction in syphilis are twofold, namely, the existence of the hypersusceptible state and the development of an exacerbation of spirochætes.

The state of hypersusceptibility is produced, as already stated, as an immunity reaction to the operation of the virus at a previous date. When present the condition will persist under favourable circumstances for years. It is known experimentally from the result of "luetin" tests that a certain degree of susceptibility develops before the onset of the acute rash, and this is no doubt due to the gradual multiplication of the virus in the tissues after infection. At the time of the rash, however, a large quantity of toxin is liberated, and this will result in a desensitization and insusceptibility which is characteristic of the secondary period following the exanthem. The liberated flood of toxin will, however, also act as an "antigen." The desensitization may be looked upon as a "negative phase," but after this has passed the state of susceptibility will reappear as the positive phase and will reach a height considerably above that present when the flood of antigen was liberated. The affected tissues will now be hypersusceptible and, in the absence of any process which might counteract this condition, will remain so for years. It is therefore clear that this state, which is found in the tertiary period, is directly due to an intoxication occurring at the time of the acute exanthem.

The second essential in the production of the hyperallergic reaction is the presence of the virus. All tissues within the body may be hypersusceptible, but no lesion will occur unless an exacerbation of the virus occurs to originate it. Some difference of opinion exists as to the source of this virus which actuates the tertiary lesion. On the one hand, the spirochætes may have remained locally in a dormant condition for many years, or perhaps they may have been "attracted" from a distant focus to an area of least resistance. It is known that certain parts of the body offer a suitable nidus for harbouring the spirochætes for many years, and it is possible that such foci are the source of those spirochætes which cause an exacerbation and produce a gumma at the site of some injury. Turnbull and one of us (P. F.) in a purely random selection of 314 *post-mortem* cases (not yet published) have found a very high incidence of syphilis in the aorta, this in many cases being the only syphilitic lesion demonstrable, and it is possible that such a focus may provide the spirochætes for gummatous processes in the skin or elsewhere. Mott has also recognized the high incidence of aortitis in asylum patients and has assumed that there is a direct causal connexion between aortitis and "parasyphilis," but from our results it is clear that

aortitis is as common, or even more common, when there is not only no "parasymphilis" but not even a syphilitic affection of the nervous system.

On the whole it is more probable that in most cases the site of exacerbation is governed by the accidental localization of the virus. The spirochætes are diffusely disseminated in the acute period and although the great majority are subsequently destroyed large numbers will remain secluded from toxic influences in relatively non-vascular areas and the walls of small vessels. These remnants will be diffusely scattered, and thus any part of the body may be the site of a spontaneous or traumatic exacerbation. Particular sites of predilection may exist, but on the other hand the frequency of lesions in particular organs may merely be due to particular strains and stresses to which these organs are exposed.

It would appear, therefore, that the hyperallergic reaction is due to two causes. Firstly, a sensitization of the area involved by toxins liberated in the acute period, and secondly, an exacerbation of spirochætes which have survived as "rests" from the general dissemination of the acute stage of syphilis. The cause of the exacerbation is unknown, but it is no doubt due to a local derangement of the balance between dormant virus and tissues. This derangement may be traumatic or may result from more subtle causes.

The Wassermann reaction.—Hypersusceptibility of the cells (hyperallergie) is not the only clinical manifestation of hypersusceptibility in syphilis; the same phenomenon may be observed in the Wassermann reaction. This reaction is, no doubt, dependent upon the degeneration of cells when specifically injured by the *Spirochæta pallida*, and it will therefore be some index of the amount of cellular destruction induced by this organism. Presuming then that a unit of "spirochæte toxin" produces relatively the same amount of cell destruction, it follows that the amount of cell destruction as evidenced by the Wassermann reaction will be proportional to the amount of "syphilis toxin" in operation. There is little reason to suppose that different strains of *Spirochæta pallida* vary largely in virulence; and therefore it is reasonable to believe that the strength of the Wassermann reaction is proportional to the number of spirochætes in the body.

This rule, however, only applies to early syphilis. During the first stages of the infection when the cells are insusceptible to the action of the toxin, no damage is produced and thus the reaction will be negative. But when, after a few weeks the susceptibility of the cells begins to

develop, an increasing number will be destroyed and thus the reaction will gradually gain in strength. The extensive lesion at the time of the rash will then account for the marked exacerbation of the Wassermann reaction which is often observed. From that time onward the spirochætes rapidly or slowly die out and the Wassermann reaction diminishes in proportion. In the latent stages a few spirochætes will be left and will produce an inappreciable lesion which may account for a slight positive reaction, or on the other hand a relatively extensive but undiagnosed internal lesion may exist together with a stronger reaction. In chronic syphilis, however, this correlation between the number of spirochætes and the strength of the reaction is absent. As is known at this time, there are very few spirochætes present, but nevertheless the Wassermann reaction is very strong, certainly as strong as it is in secondary syphilis. This lack of proportion is clearly due to the hypersusceptibility of the tissues, which leads to a great tissue destruction by a few spirochætes. This tissue destruction will occasion a strong Wassermann reaction, and thus in the tertiary stage the strength of the reaction will not be proportionate to the number of spirochætes causing it, although its presence will still indicate the effective activity of this organism.

CONCLUSIONS.

(1) The fact that relatively little cell reaction is produced by a large number of spirochætes in acute syphilis, and an extensive reaction by a small quantity of virus in chronic syphilis, is due to an alteration in the susceptibility of the tissues to the virus. The alteration corresponds to that described by von Pirquet as "allergie."

(2) The phenomena following experimental syphilization, the result of cutaneous reactions and the manifestations of syphilis itself, are all explicable on the grounds of allergie.

(3) The type of allergie, hypersusceptibility, present in tertiary syphilis is developed as an immunity response to an intoxication of the tissues occurring in the acute stage of syphilis, and the actual occurrence of the lesion is due to an exacerbation of spirochætes which have remained dormant as a "rest" from the general dissemination in the acute stage.

(4) Although an immunity response, the state of hypersusceptibility leaves the tissues abnormally susceptible to the toxic action of the virus and thus the tertiary lesion is characterized by an excessive liability to degeneration.

(5) The most important sequelæ of these degenerations are to be found in the various organs. If the interstitial tissues are the site of the lesion, the type of reaction and degeneration known as a gumma will result. This reaction is not vital and is capable of undergoing repair. If the parenchyma is involved the abortive reaction will lead to a progressive degeneration, progressive because these tissues are capable of little repair. This degeneration will lead to the functional destruction of the organ, and such a result may be occasioned even by a small quantity of virus.

CHAPTER III.—THE TISSUE REACTION IN SYPHILIS AND “PARASYPHILIS” OF THE CENTRAL NERVOUS SYSTEM.

INTRODUCTION.

Before describing the affections of the central nervous system it will be necessary to point out that we look upon the brain and spinal cord not as a “nervous system” but as one *organ* whose function is the correlation and transmission of nervous impulses. Together they correspond with the liver, kidney and other internal organs in that they are composed of a parenchyma and interstitial tissue. The parenchyma is represented by the proper nervous substance, while the interstitial tissue is of two varieties, the neuroglia and the mesoblastic interstitial tissue which is developmentally associated with the vascular structures.

THE COMPARATIVE HISTOLOGY OF THE SYPHILITIC AND “PARASYPHILITIC” LESIONS OF THE NERVOUS SYSTEM.

In reviewing shortly the lesions of syphilis as found in these organs, namely, the brain and spinal cord, it will be convenient to follow the classification already adopted in the preceding chapters dealing with syphilis generally. The “parasyphilitic” conditions will, however, be considered separately.

The central nervous system may be described as exhibiting three types of lesions: firstly, the acute lesions of the secondary period; secondly, the chronic lesions of the tertiary; and lastly, the “parasyphilitic.”

Lesions of the Secondary Period.

It has, of course, been long recognized that palsies of the cranial nerves may result from inflammatory processes involving the meninges

or bony canals during the later secondary period. Particular attention has, however, been focussed upon these occurrences since the introduction of salvarsan. It has been alleged that treatment by this drug has introduced a greater incidence of nerve lesions than was the case formerly with mercury. Very extensive investigations have been directed to this point and, although the matter may still be considered *sub judice*, the general trend of evidence undoubtedly disputes the assertion. If an apparent increase in these so-called "nerve relapses" is observed, it is in our opinion largely due to two causes. Firstly, syphilis and its treatment is now the concern of a much larger group of observers representing much wider aspects of pathology than was recently the case, and thus unusual phenomena become the subjects of discussion when formerly they excited little comment. Secondly, the salvarsan preparations are remedies so much more potent than mercury that the ordinary cutaneous relapses have become infrequent and thus such incidents as the "nerve relapses," which may be less influenced by salvarsan, become relatively more conspicuous.

In this place, however, we do not propose to enter into a discussion of this question, but to confine ourselves to the nervous affections in acute secondary syphilis, while we regard the nerve relapse, whether following salvarsan or mercury or neither, as a later manifestation of secondary syphilis.

The occurrence of a meningeal lesion at the time of the general dissemination of the virus was first insisted upon by Eduard Lang [17] in 1880. He called attention to the headaches, lassitude and even torpor which often accompany the exanthem, and ascribed these to a meningeal "irritation" which in rarer cases might even become an infiltration or definite syphilitic meningitis. In certain fatal cases of syphilitic cerebrospinal meningitis, including that recorded in 1860 by Griesinger [12], he described the lack of correlation between the extent of the lesions found *post mortem* and the severity of the symptoms during life, and argued that a definite organic meningitis was common in acute secondary syphilis, although the manifestations produced might be trivial.

To judge from the literature appearing subsequently to Lang's account, the meningitis of secondary syphilis has not attracted very general attention and, in fact, some monographs dealing with syphilis of the central nervous system omit all mention of it. The cause of this neglect probably lies in the fact that the symptoms are usually trivial and amenable to treatment and thus autopsies are rare. On the other

hand, a patient may die with acute cerebral symptoms and the connection between these symptoms and syphilis may not be recognized. At the autopsy an œdema of the brain may be noticed and histologically an infiltration of the meninges, but such a lesion need not necessarily suggest syphilis, and even if it does, there will be no conclusive proof available. At the present time, however, the nature of such diseases is made apparent by the Wassermann reaction. The enormous bearing of syphilis upon neurology tends to require the performance of this test as a routine, while the operation of lumbar puncture is of almost daily occurrence in any neurological clinic. These methods may at once disclose the syphilitic nature of an acute cerebral condition, and if the patient dies the pathologist in his search for the cause is assisted by this previous knowledge.

In recent years as a result of the more general application of the operation of lumbar puncture, attention has again been focussed upon the early syphilitic lesions of the central nervous system. Thus Ravaut [45] (1903) examined the cerebrospinal fluid of a large number of acute syphilitics, and although no obvious nervous manifestations were present, nevertheless there was evidence of "meningeal irritation" in no less than 71 out of 118 fluids examined. Similar results have since been obtained by many, but notably by Altmann and Dreyfus [1] and Fraenkel [10]. In such cases the cerebrospinal fluid may be under increased tension, may contain an abnormal quantity of albumen or, which is most striking, may show a definite lymphocytosis.

Although there has been considerable discussion as to the precise explanation of these findings, there can be but little doubt in the light of subsequent knowledge that the lymphocytosis and adjuvant phenomena are an indication of "meningeal irritation," or in more accepted pathological phraseology of "meningitis." There is reason to believe that at the time of the generalization of the virus in the early stages of syphilis the serous membranes may be affected in the same way as the mucous membranes or skin, and according to Ellis [6] such affections may be present even before the appearance of the cutaneous exanthem. Several instances of this condition are recorded in the series of Dr. Head and Dr. Fearnside. In particular we may refer to Case No. 313.¹ This female patient had acute secondary syphilis, and was observed in the fourth month after infection. No obvious nervous signs were present, but nevertheless there was a very marked pleocytosis in the

¹ For an account of this case *vide Brain*, 1914, vol. xxxvii, p. 30.

cerebrospinal fluid and also a positive Wassermann reaction. We have stated that no obvious nervous signs were present, but by the special methods of Dr. Head and Dr. Fearnside's distinct evidence of "root irritation" was obtained. In fact this patient in the early secondary stage had a marked meningitis of the spinal cord, and yet the only clinical evidences of this were a series of segmental areas showing cutaneous hyperæsthesia. We are of opinion that if a precise neurological examination of secondary syphilitic patients was made as a routine, clinical evidence of meningitis would be obtained in the majority of those patients who show pathological changes in the cerebrospinal fluid.

The relation of this meningitis to syphilis has been demonstrated by Hoffmann [13]. In a case of acute syphilis without obvious nervous manifestations he was able to demonstrate by inoculation of the cerebrospinal fluid into animals the presence of the specific virus, and thus, although in the absence of an autopsy the exact relation of the *Spirochæta pallida* to the meningeal lesion must remain somewhat conjectural, it is clear that the meningitis is an active process actually due to this organism.

In a few cases in which nervous manifestations developed somewhat later in the secondary period the presence of the *Spirochæta pallida* in the tissues of the nervous system has also been demonstrated. Gaucher, Paris and Merle [11] investigated a fatal case of hemiplegia developing seven months after infection. Perivenous collections of cells were found in the meninges of the spinal cord, and a proliferation of the endothelium of the vessels. The brain was œdematous and the meninges infiltrated. No spirochætes could be found in sections, although one was discovered in the cerebrospinal fluid. Nichols and Hough [31] also found spirochætes by inoculating into rabbits the cerebrospinal fluid from a case of hemiplegia nine months after infection, while in a similar type of case Sézary and Paillard [48] found spirochætes in the cerebrospinal fluid by the method of dark-ground illumination. Although the histology of the early secondary meningitis of adults must be described as being unknown, nevertheless it is probable that it bears some resemblance to the lesions found in infantile meningitis. Ravaut and Ponselle [46] examined a case of acute syphilitic encephalitis in an infant, and found the spirochætes situated in perivenous cellular collections. Ranke [44] also examined an infant and found large numbers of spirochætes in the lymphatics surrounding the vessels in the meninges and spreading out from the intima. A small

number of the organisms had also wandered from the neighbourhood of the vessels into the cerebral substance.

In further support of the suggestion that the nervous system is frequently involved in early syphilis, it will be permissible to refer to the researches of Steiner [50] and Jakob and Weygandt [16] upon rabbit syphilis. It will be remembered that syphilis in these animals tends to remain local and to progress towards spontaneous cure without obvious general symptoms. An infected rabbit may therefore be compared with a human being in the primary stage. Nevertheless the work of these authors shows that inflammatory lesions of the roots of the spinal nerves are constant, and even slight affections of the spinal cord and brain itself.

Lesions of the Tertiary Period.

Little difficulty is found in analysing the tissue reactions in the condition usually termed "gummatous meningitis." This is a lesion which affects the membranes of the central nervous system and also the prolongations of these membranes into the substance of the brain and cord. The term meningitis is therefore to some extent a misnomer, since the lesion may only affect the interior of the brain, while the actual coverings escape.

The gummatous process does not differ in origin from gummatous processes elsewhere. It is a granuloma forming about a small vessel, and by the confluence of a number of such foci the affected parts may be much thickened. The granuloma is formed by a proliferation of the fixed interstitial cells and an accumulation of wandering lymphocytes and plasma-cells, which may be observed in the surrounding lymphatics. The characteristic secondary changes, fibrosis and degeneration also follow.

The site of origin of the process is in the vascular tissues, and often in the walls of the cerebral vessels. The perivascular accumulations and the proliferation of the endothelium often lead to a thrombosis of these vessels, and thus the condition is sometimes referred to as "vascular syphilis"; the gummatous processes, however, in the body generally are no less "vascular" than those in the brain. Although the lesion may be widespread and involve not only the coverings of the central nervous system, but also the interior of these organs, nevertheless it appears to be confined to the lymph-vascular structures, and the nerve tissue proper is not grossly affected. Such lesions as are sometimes found may be due to a slight diffusion of the intoxication

similar to that which occurs in the parenchyma elsewhere about a gummatous process, or they may be merely due to pressure from exudates rather than a primary intoxication by the virus.

The relation of the *Spirochæta pallida* to the lesions of gummatous meningitis has been established in one case by Versé [53]. Small multiple gummata, in which central caseation was only just starting, were found in the meninges and the spirochætes were observed in the periphery of these nodules.

Among the so-called "gummatous" lesions of the brain are usually included those cases which really belong to the late secondary period and are not strictly "gummatous" at all. Thus in the case recorded by Strasmann [51] there was no gummatous process but a diffuse meningitis of the base and convexity of the brain. Large numbers of spirochætes were found in the walls and adventitial sheaths of the small vessels, which themselves exhibited endarteritis. The organisms were also found free in the meninges. The onset of the condition occurred two years after infection.

"Parasyphilitic" Lesions.

Dementia paralytica.—If we confine ourselves to the essential alterations found in early stages of dementia paralytica, we find relatively simple lesions. The pia is in a state of inflammation, thickened and unduly attached to the underlying cortex. It may be infiltrated by large numbers of lymphocytes and plasma-cells, while the fixed elements including the endothelium of the capillaries and small vessels show a slight degree of proliferation. These cells, occupying the lymph spaces of the pia, also invade and inject the adventitial sheaths of the vessels which perforate the cortex at right angles, and thus in sections these vessels are clearly marked out not only by the proliferation of the connective tissue in their walls, but also by the passive infiltration by lymphocytes and plasma-cells.

In addition to these alterations of the mesoblastic elements of the brain, changes are also marked in the ectoblastic nervous tissue and the neuroglia. The injury to the ganglion cells is particularly marked; many may be observed to be swollen, while others exhibit all stages of chromatolysis and degeneration; the number of neuroglial cells is much increased; they appear to be especially condensed in particular localities.

As is well known, the presence of the *Spirochæta pallida* in the brain in dementia paralytica has now been demonstrated by Noguchi

and Moore [36]. In their first account they were able to find the spirochætes in twelve out of seventy cases. The distribution was quite different to that noticed in the secondary and tertiary lesions, in that the spirochætes were never found in the membranes or about the vessels, but always in the substance of the brain, and sometimes in relation to the nerve-cells. No connexion was demonstrable between the position of the organisms and the distribution of the cellular infiltrations. In Noguchi's [34] second series of observations he obtained a larger number of positive results, namely, thirty-six in 130 cases. Marie, Levaditi, and Bankowski [24] have confirmed Noguchi and Moore's results. In two out of twenty-four brains examined they found spirochætes with a distribution similar to that described by Noguchi and Moore. In a subsequent publication, however [19], they also illustrated a case in which large numbers of spirochætes were present, not only within the lumen of the vessels, but also in the walls, and migrating into the surrounding nerve tissues. Marinesco and Minea [26] also described an abnormal distribution in their one positive case among twenty-six examined; the spirochætes were situated in the meninges only, and not in the brain substance; but this case was not represented to be pure dementia paralytica, but dementia resulting from syphilitic meningitis.

When Noguchi first undertook the examination of brains from cases of dementia paralytica, it was with the hope of establishing a connexion between the granules found in his cultures of *Spirochæta pallida* and similar structures present in Levaditi silver preparations, and therefore his first discovery of a single typical spirochæte was unexpected. In some Levaditi preparations, as also with the modification introduced by Noguchi, the black granules are so numerous and are so often fortuitously arranged in a linear distribution that a connection between them and the *Spirochæta pallida* is still sometimes suggested. It is therefore of importance that this organism has been demonstrated by Noguchi, Levaditi, and others by the dark-ground method, and also in stained and unstained films. If any doubt remained that the spirochæte is present in the brain in no other than its ordinary form, this should be removed by the demonstration by Forster and Tomaszewski [9] and Berger [3] of typical living *Spirochæta pallida* in material obtained by brain puncture during life.

The identity of the spirochæte found in dementia paralytica with *Spirochæta pallida* has been proved by Noguchi [35] by means of animal inoculation. He was successful in obtaining testicular lesions in the

rabbit with brain substance from one out of six cases of dementia paralytica. The lesions were of slow onset, and contained few spirochætes, but these were quite typical. Uhlenhuth and Mulzer [52] have also obtained one positive inoculation in five, while Berger [3] succeeded in producing very small testicular lesions containing *Spirochæta pallida* in three cases out of twenty. There is no doubt that the long incubation period of the experimental lesion and its ill-developed character is abnormal when compared with the results obtained with acute syphilitic material; but, on the other hand, inoculation of tertiary products produce very similar effects. The abnormality does not appear to us to warrant the assumption of a special strain of spirochætes in dementia paralytica. The chronicity of the lesion is due probably to the small number of spirochætes in the inoculated material, and, no doubt, a certain loss of virulence following the long parasitic sojourn in the body.

We ourselves have examined a series of brains for the purpose of demonstrating *Spirochæta pallida*, and also to determine the relation of this organism to the histological changes. The procedure was to examine the specimen by the dark-ground method, and then to remove a "positive" area for histological examination and silver impregnation. We are indebted to Dr. Gettings, of the West Riding Asylum, Wakefield, for the material. Among the twelve specimens examined five exhibited lesions other than those of dementia paralytica, and in these no spirochætes were found. The remaining seven were typical examples of this condition, and six times undoubted spirochætes were discoverable by the dark-ground method. When these seven cases had been fixed and stained by Noguchi's method, however, positive results were obtained in four only. These were the ones in which the organisms had been most numerous.

By the technique which we have employed, the demonstration of the *Spirochæta pallida* is not attended with undue labour, but when examining the silver sections it is desirable to search rapidly without great concentration, since the distribution of the spirochætes is relatively focal, and when one is found, others are nearly always detected in the same neighbourhood; indeed, one focus may contain so many spirochætes that they could not be overlooked, while the rest of the section is relatively free.

The organisms are practically always confined to the grey matter; indeed, we have only once detected a single example in the meninges. We have been unable to observe any constant relation to the nerve

elements or to the blood-vessels, as described by Marie, Levaditi, and Bankowski. Indeed, the distribution of the spirochætes has been quite diffuse as regards the histological features, and especially has not been confined to the area of infiltration.

All the cases examined by us had exhibited relatively acute manifestations before death, and the brains themselves were not markedly wasted. The lesions appeared to be, on the whole, recent. Unfortunately, no "history" was obtainable in any case, and therefore the duration of the infection is unknown.

Tabes.—The histopathology of tabes dorsalis cannot be said to be clearly defined. In the case of dementia paralytica there is little or no dispute as to the actual lesions present, but in tabes, on the other hand, many lesions have been described as being present which are not generally accepted as characteristic. In many cases an isolated phenomenon is assumed to be constant, while, in fact, it has been inconstant or accidental.

The indefinite and contradictory nature of these reports is due to the fact that tabes dorsalis is a chronic disease, and the findings at autopsies in cases of all stages of development have been evaluated equally as bearing upon the essential lesions. It is quite clear, however, that the appearances seen in an advanced case of tabes dorsalis will be of little assistance in arriving at the essential nature of the process. The picture will be entirely confused by secondary inflammatory and degenerative changes.

With the growing knowledge that the etiology of general paralysis and tabes dorsalis was the same, it began to be recognized that the two conditions were neither clinically nor pathologically distinct.

Numerous cases were differentiated in which the symptoms of both diseases were present, and, *post mortem*, it was found that the lesions of tabes dorsalis were common in dementia paralytica. The great importance of this discovery lay in the fact that since the patients died early of dementia paralytica, the lesions of tabes dorsalis might be studied in their earliest forms before they had given rise to obvious symptoms. In our opinion a consideration of the essential pathology of the disease must be confined entirely to these early cases.

As is well known, the most obvious initial lesion of tabes dorsalis is a degeneration of certain exogenous nerve-fibres, situated in the posterior columns of the cord, and occupying the position known as the "bandelette externe." These fibres have their trophic centre in the posterior root ganglion, and form the central mass of the posterior

roots. The lesion tends to be symmetrical on both sides, although the process is more advanced in that first affected. In addition to these long fibres, others entering the cord from the posterior roots are affected. These are short fibres, which end in the grey matter of the cord. As the process advances, the confines of the degeneration enlarge until practically the whole of the fibres arising from the posterior roots and occupying the posterior columns of the cord are affected.

Centrally the degeneration of the fibres may be followed to their arborizations, but peripherally the limit of the process is uncertain. In the earliest cases of *tabes dorsalis* it is generally admitted that there is no degeneration of the nerve-fibres in the posterior root, but, according to Nageotte [27 and 28], at a later date the extramedullary section lying in the subarachnoid space is largely degenerated. This author holds that a "radiculitis" is constant in *tabes dorsalis*, and that the vitality of the central section of the nerve is thus diminished, with the result that a degeneration starts at the central arborization, and gradually extends back towards the ganglion. At the present time it may be said that such a view is untenable. The majority of writers appear to favour the view of Redlich and Obersteiner that the degeneration of the columns takes origin at the so-called "ring of Obersteiner," an apparent constriction in the posterior root at its point of insertion into the cord. A "sclerosing meningitis" is assumed to account for an injury to the root at this point. Orr and Rows [38] also favoured this place as representing the origin of the degeneration, but pointed out that at the same spot the neurilemma which clothed the nerve in the root was reflected upon the cord. They represented this absence of the neurilemma to be the cause of the site of the degeneration, since a nerve unprotected by this covering was more open to toxic influences. In view of the extensive experimental work by which this opinion is supported, it may be taken as being substantially correct, with the reservation that the point of reflection of the neurilemma does not accurately coincide with the ring of Obersteiner. The exact spot is variable in different fibres, so that one fibre of the root may be unprotected for a greater distance than another, and thus the degeneration of *tabes dorsalis* may extend for a variable short distance into the root.

Although statements have been made to the contrary, it is probable that there is no essential lesion of the cells in the posterior root ganglion in typical cases of *tabes dorsalis*. The changes observed in

later cases are merely atrophic, and secondary to the degeneration of the columns.

An early and constant feature of tabes dorsalis is the proliferation of the neuroglia of the affected columns.

The interstitial structures are also involved in the process. The pia mater over the posterior columns is always affected, and on section is found to be infiltrated with lymphocytes and plasma-cells. Perivascular collections of these cells are also commonly found about the veins, but the arterioles are usually free from obvious changes. The meninges covering the anterolateral faces of the cord are generally normal. The slight degree of meningitis which is observed over the posterior columns is also common to a variable extent in the roots, and, indeed, has been held to be the essential lesion of tabes dorsalis, both by Nageotte and by Redlich and Obersteiner.

It cannot be denied that inflammatory lesions of the roots are common, and, indeed, an actual gummatous process may occur, but they are far from constant.

The relation of the *Spirochæta pallida* to the lesions of tabes dorsalis is at present unknown. Noguchi [34] has indeed mentioned the presence of the organism in the posterior columns of one case, but, on the other hand, Versé [53] has described spirochæte-like bodies in two cases—in one in the posterior root and in the other in the ganglion. It would appear that the subject requires further investigation.

In addition to the lesions of classical dementia paralytica and tabes dorsalis, other so-called "parasyphilitic" diseases of the central nervous system are described which differ from the two main types chiefly in the area of the brain or cord involved. Thus "tabes optica" denotes a "parasyphilitic" lesion of the optic nerves. The microscopic anatomy of such lesions has been studied by Stargardt [49]. He failed to find evidence of a degeneration originating in the retina. In every case there was present an inflammatory lesion of the optic chiasma which was associated with a degeneration of the nerves at this point. The inflammation as evidenced by the type and distribution of the interstitial cells was of exactly the same nature as that observed in dementia paralytica. The degeneration of the nerves did not precede the inflammation, neither did the inflammation precede the degeneration; they were both coincident processes, due in all probability to the same cause, the *Spirochæta pallida*. Stargardt was, however, unable to demonstrate this organism.

If allowance is made for the relative obscurity of the morbid histology of tabes dorsalis as compared with that of dementia paralytica, it will be recognized from the foregoing account that the two processes are closely comparable.

In tabes is found a profound degeneration of nerve structures and an overgrowth of glial tissue. This is the outstanding lesion, but, in addition, there is a constant lymphocyte and plasma-cell infiltration of the neighbouring meninges and perivascular cell accumulations. These lesions are also the lesions of dementia paralytica, and the close similarity between the histology of the two diseases had already led many to accept the theory of a common etiology before the demonstration of the *Spirochæta pallida* in both rendered such a view almost unavoidable.

THE COMPARATIVE PATHOLOGY OF THE SYPHILITIC AND "PARASYPHILITIC" LESIONS OF THE NERVOUS SYSTEM.

In the preceding section we have described three groups of diseases of the central nervous system which are due to syphilis; namely, the lesions of secondary syphilis, meningitis or encephalitis; the tertiary processes, so-called "gummatous meningitis," with which are usually associated the later secondary manifestations, and finally the "parasyphilitic" conditions, dementia paralytica, tabes dorsalis and other varieties. The question now arises, what is the relation between these three groups?

Secondary Syphilis of the Nervous System.

Although it must be admitted that the precise pathology of the early syphilitic lesions of the brain and spinal cord already referred to is a field of neurology which requires much elucidation, nevertheless it is clear that they may be divided into two main groups, an acute condition which rapidly leads to stupor and death, and a subacute lesion which may only be indicated by irritability and headache. In the latter there is no indication of an affection of nerve-cells; it is probably due entirely to a slight meningitis, that is to say to a slight meningeal or interstitial infiltration due to the presence of spirochætes about the vessels in the membranes. On the other hand, in a more acute lesion, the spirochætes may wander from the lymphatics surrounding the vessels in large numbers and may invade the actual neurons of the brain. In this way true encephalitis may arise and according to its severity or distribution may give rise even to fatal symptoms.

In the secondary period, therefore, the brain may be looked upon as being prone to a subacute lesion which mostly affects the interstitial tissues and also an acute lesion of greater extent which involves not only the interstitial but also the parenchymatous structures. In this manner it may be said that the early lesions of the brain are very similar to those of the liver; on the one hand is the acute parenchymatous lesion leading to acute atrophy and death, and on the other the interstitial inflammation which may only be detected by the occurrence of a slight jaundice.

The later secondary affections of the brain and cord may be looked upon entirely as interstitial lesions. They are associated with more infiltration and proliferation than the early lesions and thus lead to secondary interruption of nerve structures, and consequently to well-marked localizing signs—cranial palsies, root lesions, &c.

Tertiary Lesions of the Central Nervous System.

The relation of these affections to the tertiary affections of other organs is close. They consist of foci, relatively discrete or fused, which develop about a blood-vessel as a result of an exacerbation of spirochaetes in or about its walls. The process is essentially focal, although the conglomeration of foci may lead to a diffuse result; but, however diffuse, there is very little tendency for the lesion to progress beyond the confines of the interstitial tissues in which it takes origin. The common name "gummatous meningitis" is, however, incorrect, in that the inflammation may extend from the meninges along the perforating vessels into the brain or cord, and, indeed, in rare cases these vessels may be involved alone while the meninges escape.

It is probable that when evidence of nerve degeneration is detected, this is a secondary process due merely to pressure of exudates or interruption of blood-supply. In the case of the liver there is indeed a primary destruction of such parenchymatous cells as find themselves within the zone of toxic influence, but in the nervous system, as will be noticed later, there is a sharper anatomical separation between parenchymatous and interstitial tissues, and therefore the gummatous process tends to be more purely interstitial than in other organs.

If, however, allowance is made for slight differences due to variety in anatomical structure, it is clear that the gummatous lesions of the central nervous system are strictly analogous to those chronic focal processes in the various internal organs in which the incidence of the

intoxication falls almost entirely upon the interstitial tissues, e.g., the more or less focal "gumma" of the liver. The expression "gummatous meningitis" may, therefore, be correctly superseded by the term "chronic syphilitic interstitial encephalitis or myelitis."

"Parasyphilis."

While the gross and microscopic appearances of brains and spinal cords affected with "parasyphilis" are on the whole well known, the exact nature of the process is very much *sub judice*. The literature dealing with this subject is enormous, and it will be possible to deal only with the question in its broader aspects. The reader who requires a detailed survey of the relation of "parasyphilis" to syphilis may be referred to the Report of Nonne to the Section of Neuropathology of the recent International Congress of Medicine [37].

It would appear that one group of pathologists, especially perhaps those of the French school, look upon dementia paralytica as an encephalitis, or *inflammation* of the brain, while others, German and English, hold the view that the whole process is *degenerative*.

With regard to the "*inflammatory*" theory opinion is divided as to the primary lesion, that is to say many hold that the nervous tissues proper are the seat of the initial lesion, while the increase and activity of the interstitial tissues and neuroglia is secondary. This group favours the term parenchymatous encephalitis. Others, on the other hand, hold that the initial process is interstitial, perhaps vascular or lymphatic, and this leads to a secondary degeneration of the nerve elements.

Those who hold the "*degenerative*" view assume a pathological process which must be looked upon as abnormal. They consider that the degeneration of the nervous tissue is *primary* and is not the result of an antecedent inflammation. Although it is difficult to find examples of primary degeneration in other fields of pathology, it is assumed that the nerve-cell, being a highly specialized structure, is abnormal and can undergo this process simply as a result of unfavourable environment of long standing. According to this view the proliferation of neuroglia is secondary, and the meningeal and perivascular changes are of the same nature.

The precise effect of syphilis in the causation of the brain lesions appears to lead to as much dispute as does the interpretation of the lesion itself.

On all sides it is admitted that syphilis is an essential in the etiology of the disease, but as to whether the *Spirochæta pallida* is the immediate

irritant, or whether the process results from a hitherto unrecognized ultimate effect of this organism is not definitely known.

Those who hold the "inflammatory" view, whether interstitial or parenchymatous, presume a direct activity of the spirochæte exercised in an abnormal form, while the "degenerative" theory presumes that a weakness of the cells results from a "constitutional syphilis" or prolonged action of "toxin," and that the actual degeneration is occasioned by accessory factors of stress (alcohol, trauma, "exhaustion," &c.). In general the type of lesion is considered not to be "syphilitic."

Recently the concept of "parasyphilis" as an active syphilitic lesion has been supported by Stargardt [49]. This author found the "parasyphilitic" lesions of the optic nerve to be due to a chronic inflammation of the same type as that found in the brain in dementia paralytica, an inflammation due to the virus of syphilis. Again, Schoenborn and Cuntz [47] disputed the existence of a "parasyphilis" in the sense of Fournier; they pointed out that the concept rested almost entirely upon the incurability of the condition and the difficulty in demonstrating the virus. Cuntz [4] argued that most of the "parasyphilitic" diseases of Fournier in the internal organs are now known to be actively syphilitic, and therefore that the nervous lesions were probably of the same nature.

From our analysis of the essential cell reactions of syphilis in Chapter I, it will be seen that one of the chief characteristics of these reactions is the perivascular distribution. A small vessel is found with a proliferated endothelium, the local fixed connective tissue cells are also proliferated while the surrounding lymphatics are laden with plasma-cells and lymphocytes. This is the reaction of the interstitial cells. Turning now to the account of the histology of "parasyphilis" it will be seen that the interstitial reaction in the meninges and about the vessels is closely analogous. Thus in our view the interstitial lesion of parasyphilis may be described correctly as "syphilitic." Again, on consideration of the nerve lesion and neuroglial proliferation in these cases we find striking resemblances to those tertiary syphilitic lesions of internal organs in which, owing to a diffuse distribution of the virus, the parenchymatous lesion is more striking than the interstitial, and we have evolved the view that the lesion of parasyphilis is a tertiary syphilitic parenchymatous inflammation, not of an abnormal or "nongummatous" type, but of essentially the same nature as parenchymatous lesions of all organs due to tertiary syphilis [22 and 23].

Dementia paralytica.—As we have already pointed out in the case

of the liver and other organs the *Spirochæta pallida* produces parenchymatous and interstitial reactions in all cases, but in some the effect may be most marked upon the parenchyma, while in others upon the interstitial tissues. These different effects are due to the distribution of the spirochætes. In those organs in which parenchyma and interstitial tissues are closely related, the two types of reaction will be somewhat confused and will commonly occur together in the same process.

In the case of the brain, however, we would point out that the parenchymatous nerve tissues, together with the neuroglia, are developmentally and anatomically separated from the interstitial tissues proper, that is, the vascular-lymphatic structures. In the process of development the vessels grow from the meninges into the cortex and push before themselves the innermost layer of the pia and the limiting neuroglial membrane of Lenhossek. These tissue layers are represented by the wall of the perivascular adventitial sheath and the insertions of the neuroglia upon it, and these structures form a barrier more or less impenetrable between the lymphatics in the adventitial sheath and the ganglion cells and neuroglia.

Thus in the brain there is an abnormal separation of parenchyma and interstitial tissues, and this will lead to an unusually distinct effect of the *Spirochæta pallida* upon the two tissues according as it finds itself on one side or other of the anatomical barrier; if in the nervous tissues the chief lesion will be parenchymatous, if in the lympho-vascular tissues the lesion will be chiefly interstitial.

Now from the recent researches of Noguchi and others it is established that the spirochætes in dementia paralytica tend to be limited to the nervous tissues and are rarely found in the lymphatics or meninges, thus it is clear that the chief effect of the organism will be expended upon the ganglion cells and neuroglia in the brain substance proper.

According to our view an exacerbation of the virus in the brain leads to an immediate reaction in the sense of inflammation of the nerve-cells and neuroglia. The swelling of the ganglion-cells may mark this reaction and may be equivalent to the "cloudy swelling" of other inflamed parenchymatous cells. The reaction will, however, be abortive; the intoxication will be greater than the cells can sustain and a *secondary* degeneration will soon set in. The neuroglia may be looked upon as a special type of interstitial tissue and the reaction in this case will lead to a proliferation. This process is equivalent to a reaction of fixed interstitial cells. Since now a toxic focus is in

a state of activity the wandering cells will be attracted to the area from the surrounding lymphatics. These cells, lymphocytes and plasma-cells, will be found in the lymphatics of the meninges and perforating vessels streaming towards the focus. They cannot, however, attain it in the brain as they can in other organs, owing to the more or less impenetrable barrier already referred to; thus the process will tend to remain diffuse and no localized collection of cells or gumma will be produced, neither will the distribution of the spirochaetes correspond to that of the cell infiltrations, as we have already observed. No doubt, a certain degree of proliferation of the fixed cells in the lymphatics will occur in some cases owing to diffusion of the toxin or a wider distribution of the spirochaetes, but the general active effect in the lymph-vascular tissues will not be marked, the process there will be more or less passive. The amount of active reaction of the interstitial cells will depend upon the chronicity of the disease. In the most rapid cases it will be least pronounced.

According to the view enunciated the lesion of dementia paralytica is as typically syphilitic as a lesion of the liver. It occurs as an inflammatory reaction about the *Spirochæta pallida* situated among the nerve-cells, but its effect is most marked upon the parenchyma because this tissue is abnormally distinct from the interstitial tissue. A reaction of the parenchyma rapidly leads to degeneration as in the liver, while the reaction in the fixed neuroglial tissues produces proliferation. The wandering cells fill the lymphatics as in other organs, but cannot reach the toxic focus and so produce a "gumma."

We therefore refer to dementia paralytica as a tertiary syphilitic parenchymatous encephalitis, and had already arrived at this conclusion before the demonstration by Noguchi of the *Spirochæta pallida* in the brain. We were of the opinion that, in view of the technical difficulties experienced in applying Levaditi's staining method to the brain, the mere fact that the virus could not be demonstrated was a matter of little importance.

Tabes dorsalis.—In dementia paralytica we have described the lesion as an inflammatory reaction of the nerve-cells and neuroglia, and, to a slight extent, of the lymph-vascular tissues to the stimulus of the *Spirochæta pallida* situated among the nerve-cells. In our view the essential lesion of tabes dorsalis also is due to an inflammatory reaction on the part of the nerve-fibres and neuroglia induced by the presence of the *Spirochæta pallida*. As in the case of the brain, the neuroglia will proliferate, but the intoxication of the nerve-fibre will lead to its

destruction. Some degree of reaction may be observed in the fixed lymph-vascular tissues, and the lymphatics of the meninges will be infiltrated by wandering cells as already described in dementia paralytica.

The degeneration of the nerve-fibres following on this intoxication will occur in those parts only which have been deprived of the neurilemma. It is known that the neurilemma is a structure of primary importance in the regeneration of nerves, and it is probable that it also exerts a protective and nutritive function, and thus if a sublethal intoxication of a neuron occurs the part which is unprotected by the neurilemma will suffer, rather than the protected portion. In this manner it is easy to account for the fact that the degeneration ceases where the neurilemma clothes the nerve, as pointed out by Orr and Rows [38].

These authors were able to show that in early cases of dementia paralytica changes were always present in the cord which were identical with those found in the earliest lesions of tabes dorsalis. These changes consisted of parenchymatous degenerations of the posterior columns, and in every instance the degenerative lesion originated at the point of loss of the neurilemma. From other papers by the same investigators it is clear that exactly similar cord lesions or lesions of the comparable cranial nerves may follow spontaneously as a result of an intoxication of the spinal cord or brain by the products of septic foci situated in the skin [39], and indeed such lesions may be produced by introducing bacterial toxins into the perineural lymph channels of the afferent nerves [40]. In all such cases in which a "tabetic" lesion is produced by a peripheral septic focus, the toxins ascend to the posterior columns of the cord by the lymphatics of the peripheral nerves without these nerves being themselves obviously injured. The existence of this afferent perineural lymphatic system had been previously noted by Homén and Laitinen [14] and was confirmed by Orr and Rows. On these grounds Orr and Rows [41] have looked upon dementia paralytica and tabes dorsalis as chronic inflammatory lesions due to a toxic substance ascending the lymph-stream; in any case it is clear from their work that the morbid agent which induces the degeneration is distributed by the lymphatic rather than by the blood-stream, and indeed the same conclusion had already been stated in much less detail by Marie and Guillain [25]. Tabes dorsalis was a lesion of the lymph system which comprised the posterior columns, the membranes covering them and the posterior roots.

Since therefore the parenchymatous degeneration and also the adventitial changes of tabes dorsalis and dementia paralytica, namely the proliferation of the glia and the plasma-cell and perivascular proliferation, may all be produced experimentally by the introduction of bacterial toxins into the afferent lymphatics, it is clear that the *Spirochæta pallida*, operating in the same anatomical areas, may be assumed to be the actual cause of the two diseases under discussion, especially when it can be shown that the lesion produced is strictly comparable to the lesions produced by the same virus in other internal organs.

CLASSIFICATION OF THE SYPHILITIC DISEASES OF THE CENTRAL NERVOUS SYSTEM.

According to the views expressed in the previous pages "parasyphilis" has no separate existence from the other syphilitic diseases of the central nervous system so far as its pathology is concerned. It is a tertiary process resulting from a more or less diffuse distribution of spirochætes within the nervous tissues as opposed to the gummatous lesions which result from an inflammation located in the interstitial tissues. These two are similar lesions occurring in different tissues and thus leading to very different results. If the "gummatous meningitis" of the brain may be referred to as "chronic interstitial encephalitis" so may "parasyphilis" be described as "chronic parenchymatous encephalitis or myelitis."

Although the processes are often distinct, nevertheless there is reason to believe that they are quite commonly combined. "Meningitis," for instance, is frequent in tabes dorsalis. In such cases it may be assumed that the distribution of the spirochætes is more general than usual; they may be present both in the meninges and also in the brain substance, and thus may produce both types of "tertiary" lesion at the same time.

We have already stated [8] that an associated parenchymatous and interstitial lesion may be assumed when, as a result of treatment in "parasyphilis," the Wassermann reaction in the cerebrospinal fluid is rapidly reduced in intensity up to a certain point beyond which it is persistent. Such cases are relatively common, and we have recently been able to observe *post mortem* the accuracy of this assumption. On reference to Case 90¹ it will be seen that the reaction behaved in this

¹ A reference to this case will be found in *Brain*, 1914, vol. xxxvii, p. 124.

manner, and at the autopsy a typical dementia paralytica was disclosed but associated with a marked interstitial lesion.

The relationship between the lesions produced by syphilis may, therefore, be tabulated as follows:—

Lesions of the Secondary Period.

- (1) Interstitial encephalitis or myelitis ("meningitis").
- (2) Parenchymatous encephalitis or myelitis ("encephalitis," "myelitis").

Lesions of the Tertiary Period.

- (1) Chronic interstitial encephalitis or myelitis ("gummatous meningitis").
- (2) Chronic parenchymatous encephalitis ("dementia paralytica").
- (3) Chronic parenchymatous myelitis ("tabes dorsalis").

CONCLUSIONS.

We have shown that the central nervous system is affected by syphilis at the same periods and in the same manner as are other internal organs. In addition the "parasyphilitic" lesions are also of a typically syphilitic nature, being directly comparable to the parenchymatous affections found elsewhere in the body. They are "tertiary" lesions differing only from the so-called "gummatous" processes in the central nervous system in that their localization is in the parenchyma while that of the latter is in the interstitial tissues.

CHAPTER IV.—ALLERGIE IN THE SYPHILITIC DISEASES OF THE NERVOUS SYSTEM.

In describing the syphilitic lesions of the internal organs we have shown that the amount and to some extent the quality of the reaction to the *Spirochæta pallida* is variable in the different stages of the disease. In the acute stages when the number of spirochætes is maximal, the tissue reaction is relatively slight, while in the chronic conditions a very marked and destructive lesion occurs although the number of causative spirochætes is small. This result is due to an alteration in the susceptibility of the tissues, called by von Pirquet "allergie."

The same disproportion between cause and effect is noticeable in the syphilitic lesions of the brain and spinal cord.

In the encephalitis of the secondary period the amount of cell reaction is slight, and yet there is reason to suppose that the spirochætes

present in the brain are as numerous as in other secondary conditions. In the tertiary interstitial encephalitis, on the other hand, the spirochætes are relatively few, although the reaction of the tissues is great. Again in the chronic parenchymatous lesions, dementia paralytica and tabes dorsalis, the extent of the lesion is great and yet the number of spirochætes is usually, as is well known, extremely small. There is thus the same lack of relation between the extent of the lesion and the amount of the virus as is observed elsewhere in syphilitic lesions. Those of the central nervous system are also under the influence of allergie.

As already described in previous chapters, the state of hypersusceptibility of the tissues generally, follows as an immunity response to the destruction of spirochætes at the time of the exanthem. In order to apply this argument to account for the chronic interstitial and parenchymatous nerve lesions, however, it will be necessary to bring evidence of a previous syphilitic inflammation of these regions during the acute stage, since the tertiary exacerbations are due to spirochætes which have remained dormant *in situ*, affecting tissues which have been previously sensitized. Such a previous involvement has already been described as a slight encephalo-myelitis occurring in the secondary stage. The lesion may be of such an intensity as to lead to appreciable symptoms; on the other hand, it may be so slight as to escape direct notice and is then merely a factor in the production of the syphilitic cachexia. Since the virus is blood-borne and part of the general dissemination during the acute stage, the interstitial tissues of the brain are mostly affected, and therefore the interstitial tissues will most often bear the brunt of the subsequent exacerbation as found in "gummatous meningitis."

It may, however, be readily understood that in certain patients a few of the spirochætes may wander from the adventitial lymph sheaths of the vessels and actually penetrate the confines of the ganglion-cells and neuroglia. The primary nervous affection in such a case may be too slight to produce noteworthy manifestations, but it may, nevertheless, be sufficient to determine the site of the exacerbation in the parenchyma at a later date and the production of dementia paralytica.

One of the chief objections which have been advanced against the inflammatory view of "parasymphilis" is the curious localizations of many of the lesions in "systems" of nerves, but a possible explanation may be found in the work of Orr and Rows. It will be remembered that these authors have demonstrated the existence of a direct lymphatic path from the skin to the central nervous system along the afferent

nerves, and by introducing bacterial toxins into this lymphatic system they have produced central lesions which are directly comparable to those of dementia paralytica and tabes dorsalis. Further, in certain chronic skin lesions (bed sores) they have observed the spontaneous development of such central lesions, and have put forward the view that the parasyphilitic diseases are due to a chronic inflammation of lymphogenous origin. The bearing of these results upon the localization of certain manifestations of "parasyphilis" is important.

The skin in secondary syphilis is, even in the absence of a rash, the site of innumerable spirochætes, and judging from the accounts of Ehrmann [5] and Levaditi [20], in which they described the *Spirochæta pallida* lying in the nerve-sheaths of the primary sore, it may be assumed that these spirochætes readily find their way into the sheaths of the nerves in secondary syphilis also. In this manner they gain a direct path to the central nervous system, as was, indeed, pointed out by Ehrmann, and since the lymphatics follow the course of the nerves it is easy to understand that the distribution of the subsequent "parasyphilitic" exacerbation will follow that of systems of nerves.

Although we consider that the blood-borne secondary encephalitis is the more probable explanation of the distribution of the lesion in dementia paralytica, it is clear that some of the more localized "parasyphilitic" lesions (primary optic atrophy, &c.) are more readily explained on the lymph-borne theory of Orr and Rows. Spirochætes derived from the skin of the face, the buccal cavity or tonsils may easily reach central areas by way of the cranial nerves and there lie dormant. An exacerbation at a later date will then develop into a local tertiary gummatous lesion if the virus is confined to the lymphatics, or a tertiary parenchymatous lesion if a few spirochætes have wandered from the lymphatics into the nervous substance proper.

The peculiar distribution of the tabetic lesion has always given rise to much discussion; but since the skin in the secondary period and also many of the internal organs harbour the spirochæte, it is easy to assume that these organisms may reach the posterior columns of the cord by the afferent perineural lymphatics and induce a slight myelitis in this position which usually escapes notice. Further, as in the brain, a few of the spirochætes may wander from the adventitial lymphatics and actually affect the nerve-fibres themselves. If such a distribution occurs a later exacerbation of these spirochætes will produce the large reactive lesion and subsequent degeneration which occasion the symptoms of tabes dorsalis. There is, in fact, very direct evidence that

such a lymphatic inflammation is common in the secondary period without producing symptoms. As is well known, syphilis in the rabbit is apparently a local disease which proceeds to spontaneous cure, and yet Steiner [50] has examined a number of these animals and found inflammatory lesions of the perineural lymphatics of the roots, which spread into the cord as adventitial collections of cells. Analogous lesions were found in the brain. The distribution of those lesions in the lymphatics is highly suggestive that the virus ascended the afferent nerves, as described by Orr and Rows in the case of bacterial toxins.

It will be understood that we have introduced the concept of a sensitization of the nerve tissues merely in order to account for the remarkable extent of the lesion which follows at a later date as a result of an exacerbation of a relatively small number of spirochætes, but nevertheless a lesion of a similar type might conceivably follow from a chronic absorption of toxin from the lymph system in the sense of Orr and Rows.

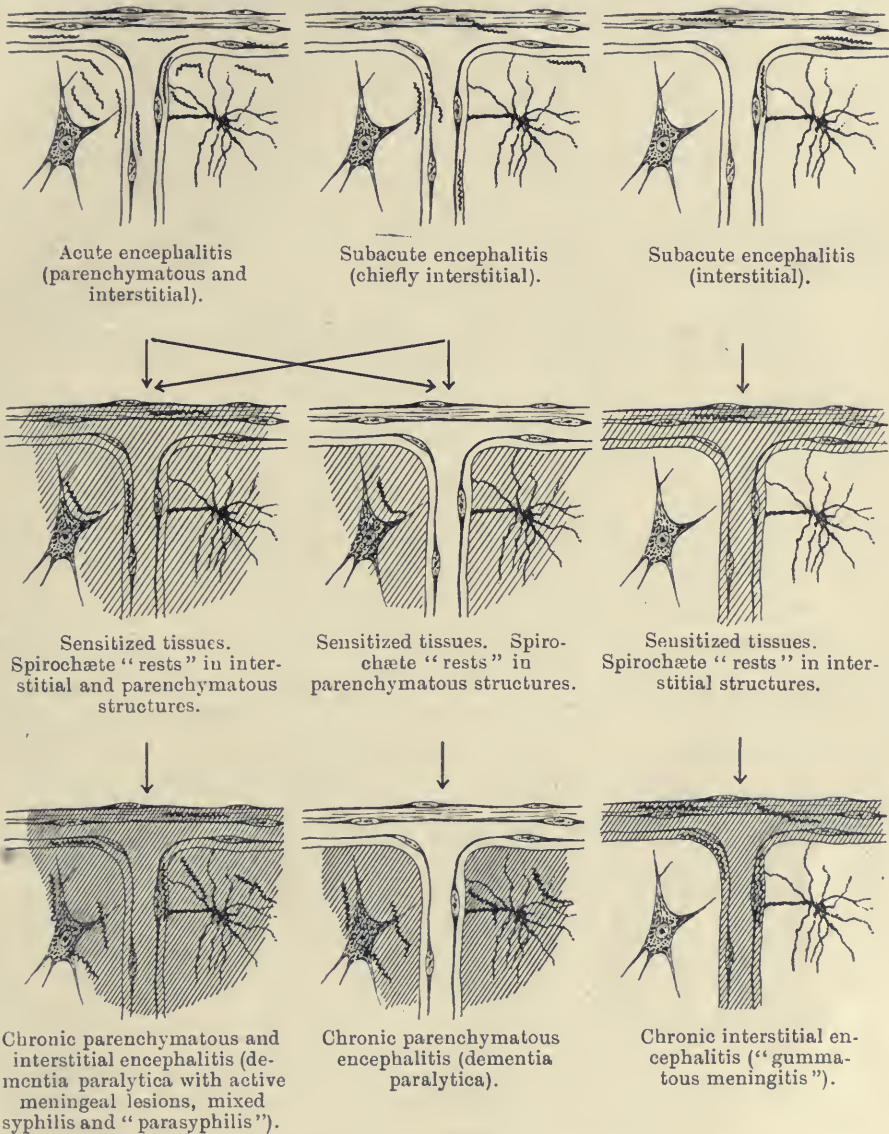
The lesions of the spinal cord produced experimentally by Orr and Rows resulted from the absorption of diffusible toxin derived from pathogenic bacteria and not from the activity of the bacteria themselves. In the case of syphilis, however, it is doubtful whether a "toxin" exists of such potency that it can effect a profound lesion at a distance. If, however, in the theory of Orr and Rows we insert the word "virus," instead of "toxin," it would follow that tabes dorsalis and dementia paralytica might be the result of a very chronic syphilitic inflammation of the special lymphatic system. The objection to such a view is that there is no source for this virus except in the secondary period, and it would seem improbable that a chronic action would continue during the whole interval of time between the secondary period and the onset of tabes dorsalis or dementia paralytica without producing symptoms.

The lesion of early tabes dorsalis and dementia paralytica appears to be too acute to be explained by an extremely slow irritation lasting many years. It suggests an exacerbation, and since the number of spirochætes causing this exacerbation must be small, we endow the issues with the state of hypersusceptibility and have adduced considerable evidence that such a state is general in chronic syphilis.

CONCLUSIONS.

The "parasyphilitic" diseases are due to an exacerbation of *Spirochæta pallida* about nerve elements which are in a state of hypersusceptibility. This state is induced as a reaction to an intoxication

DIAGRAMS OF THE EFFECT OF ALLERGIE UPON SYPHILITIC LESIONS OF THE CENTRAL NERVOUS SYSTEM (BRAIN).



Each diagram represents schematically a section of the cerebral cortex. A nerve-cell on the left hand is separated from a neuroglia cell on the right hand by a vascular prolongation of the meninges which form the upper boundary of the figure. Spirochaetes are represented by wavy lines.

The top row of figures represents the conditions in the early period of syphilis in which a variable number of spirochaetes act upon non-sensitized tissues.

In the second row of figures the shaded parts represent the various sensitized tissues in which "rests" of spirochaetes are lodged (latent period of syphilis).

In the third row of figures these sensitized areas are now thrown into reaction by the renewed activity of the spirochaetes.

occurring in the secondary period, and the spirochaetes taking part in the exacerbation are remnants of those which produced the original intoxication.

The path of invasion of the central nervous system may be twofold. Firstly, the spirochaetes may reach the nerve elements by the bloodstream as part of the general dissemination of the secondary period, or secondly, they may reach these structures during the same period by direct spread up the perineural lymphatics. The interstitial nervous lesions of tertiary syphilis are due to a similar process affecting these tissues only.

CHAPTER V.—THE EFFECT OF TREATMENT UPON SYPHILITIC DISEASES OF THE NERVOUS SYSTEM.

In previous sections we have endeavoured to show that fundamentally the lesion of "parasyphilis" is an inflammatory process in every way comparable to the other lesions of syphilis, and it will therefore be necessary to inquire into the conditions which permit of successful treatment in the one case, but not in the other.

It will be remembered that the incurability of the "parasyphilitic" lesion constituted one of the main distinctions from syphilis according to the original view of Fournier, and this standpoint has been accepted by most authorities up to the present day, to such an extent that, before the introduction of salvarsan, to apply antisypilitic treatment to a patient diagnosed as suffering from a "parasyphilitic" condition was the exception.

When the concept of "parasyphilis" as introduced by Fournier is examined, it must be generally admitted that the definition is peculiarly crude. Thus he classes under this heading not only *tabes dorsalis* and *dementia paralytica*, but also pigmentary syphilides and a large number of syphilitic and non-syphilitic states which are now entirely forgotten in this connexion. The only discoverable similarity between the parasyphilitic conditions of Fournier is a common, but not essential, derivation from syphilis and a general insusceptibility to antisypilitic treatment. At a later date (1903) very much the same attitude was adopted by Hermanides, but in his classification a further series of pathological states were included, such as chronic superficial glossitis and amyloid degeneration of the internal organs.

The concept of "parasyphilis" as propounded by Fournier and Hermanides has lately been investigated by Cuntz [4]. This author

shows in detail that the application of the term "parasyphilis" to certain diseases of internal organs is fallacious, since these diseases are purely syphilitic and directly due to the *Spirochæta pallida*.

We therefore discard the original definition of "parasyphilis" and discuss it in its modern aspect as relating to diseases of the nervous system only.

As already mentioned, the most pronounced distinction between "parasyphilis" and syphilis is the futility of antisymphilitic treatment in the former case. The disease is looked upon as being progressive in spite of the most drastic treatment, even applied in the earlier stages, and in fact it has become the common practice to omit such treatment as being useless and sometimes leading to undesirable results.

When the nature of the "parasyphilitic" lesion is considered, the reason for this futility is clear. The symptoms of dementia paralytica and of tabes dorsalis are due to degeneration of nerve elements situated in the central nervous system, and since such structures have no power of regeneration, no remedial measures can prevent the progress of the degeneration to the furthest limits of the neuron.

Such an effect is not, however, in any way characteristic of "parasyphilis" alone, since the same result follows any other lesion of the central nervous system and all such are equally refractory to treatment. Neither is the progressive degeneration of the neurons characteristic only of the central nervous system. The nervous tissue is merely the highly specialized parenchyma of the brain and is comparable to the highly specialized parenchyma of other organs. It may be taken as a general rule that the more a cell is specialized for a particular function, the less developed is its power of resistance to injury or of regeneration. The parenchyma of the liver and kidney, for instance, display a similar "delicacy" to that of the brain. The cells of these organs, when injured beyond a certain point, degenerate and eventually may be entirely replaced by fibrous tissue; no amount of mercury will "cure" a chronically inflamed kidney in the sense that it will produce a *restitutio ad integrum* of the secreting tubules. The kidney and liver, however, differ from the central nervous system in that they contain a large number of cells performing the same function, and therefore a destruction of many of these will produce no obvious effect. Their work will be undertaken by the remaining cells. Further, these organs may not only respond by an increased functional activity per cell, but an actual new formation of cells may occur. In the central nervous system, however, not only is no new formation of cells observed, but

function is so specialized that a destruction of any group of cells will immediately lead to outward manifestations of the lesion. Perhaps the nearest parallel to the nervous system is found in the testicle. A diffuse parenchymatous lesion of this organ is immediately recognized by sterility. The degeneration of the cells is progressive and is not affected by antisiphilitic treatment, so that a lesion of a certain intensity will lead to a complete loss of the spermatogenic function.

The incurability of the symptoms of dementia paralytica or tabes dorsalis does not therefore call for any further remark than does the sterility following syphilitic orchitis. If the one is to be termed "parasymphilitic" the name will equally apply to the other; but no useful purpose will follow such application, and if the term is held to imply any pathological state other than a secondary parenchymatous degeneration following injury, we hold that it should be discarded. Again we look upon the expression "progressive" as applied to "parasymphilitic" diseases as not strictly accurate. The intention is to show that dementia paralytica or tabes dorsalis once started will proceed to death. Strictly, however, the term is only applicable to the condition of each affected neuron. The degeneration of each neuron once started will be progressive until the whole unit is destroyed, but the process will not necessarily spread to contiguous neurons. To illustrate this fact it is only necessary to call attention to certain cases of primary optic atrophy and other "parasymphilitic" diseases of isolated nerve groups which do not progress. The apparent progress of the lesion in dementia paralytica and tabes dorsalis is clearly due, not to a spread of the degenerative process from neuron to neuron, but to a continued activity of the primary intoxication which leads to the secondary degeneration, in fact to *a continuation of the syphilitic inflammation in spite of treatment*.

Before discussing this aspect of the problem in more detail it will be necessary to inquire to what extent the futility of antisymphilitic treatment is completely established.

Before the era inaugurated by the epoch-making discoveries of Ehrlich and Wassermann, the treatment of "parasymphilis" was almost entirely symptomatic or palliative for the reason that the essential relation between syphilis and parasymphilis was not always accepted and because the relatively feeble antisymphilitic remedies of that time were ineffective. Since the introduction of the Wassermann reaction, however, few are found who dispute the dependence of "parasymphilis" upon syphilis, and in addition a large number of authors have described

a definite beneficial effect of salvarsan. In our view some at least of these successful therapeutic results must be ascribed to a confusion of diagnosis between "parasyphilitic" and "true syphilitic" diseases of the nervous system. It cannot be denied that in certain cases the differential diagnosis is extremely difficult and any marked and lasting improvement in a supposed case of "parasyphilis" should at once call for further investigation into the symptoms upon which the diagnosis has been based. On the other hand marked improvement in the condition of a "parasyphilitic" may be due to the resolution of an interstitial nervous syphilis associated with the parenchymatous condition. In the series of Dr. Head and Dr. Fearnside several such cases of mixed "parasyphilis" and syphilis will be observed in which as a result of treatment, or even without, the condition of the patient much improved. This recovery is accompanied by a quantitative diminution in the strength of the Wassermann reaction in the cerebrospinal fluid and a decline in the cell count, but the clinical and pathological improvement is apt to proceed only to a certain point, when the condition again becomes stationary. One such patient (case 90) died of dementia paralytica, and at the autopsy the marked interstitial lesions were demonstrated. We have, therefore, formed the opinion that when a case of "parasyphilis" shows definite pathological improvement after treatment, this result is due, not to any great alleviation in the "parasyphilitic" lesion, but to a resolution of an associated interstitial syphilis.

In general we consider that antisyphilitic treatment of pure dementia paralytica, for instance, is futile, but this result is very largely due to the fact that the nerve degeneration is of such a distribution that vital functions are early involved. The lesion even in its earliest stage is hardly compatible with continued life. In the case of tabes dorsalis, however, the outlook is different. In an early stage the nerve lesion is not necessarily fatal, and if it were possible to arrest the syphilitic process, which accounts for the progress of the lesion, it would be possible to cure tabes dorsalis; that is to say, to leave the condition *in statu quo*.

In view of the chronicity of this state it is impossible to judge to what extent this result is possible at the present day, but many must have succeeded by repeated salvarsan injections during the past two or three years in maintaining early cases of tabes dorsalis in a stationary condition.

Although, therefore, it will be generally admitted that "parasyphilitic"

states are undoubtedly refractory to treatment, it does not follow that such treatment is entirely without effect. In the paper dealing with a study of the Wassermann reaction in such conditions [7] it will be seen that we have been unable to show any definite result of treatment, as evidenced by a diminution of the strength of the Wassermann reaction in the cerebrospinal fluid, nevertheless it will be observed that after lapses of time longer than we have been able to record in any fresh case, the reaction may be found to be negative, and this finding will coincide with a stationary condition of the manifestations. If the activity of the disease may subside naturally, it is not unreasonable to suppose that this subsidence may be assisted by treatment.

If, then, it is allowed that therapeutic measures may have some beneficial effect, it is still anomalous that this effect should be so small compared with the rapid improvement in cases of cerebrospinal syphilis, in particular when we have described the two processes as being fundamentally the same.

We have already shown that a tertiary interstitial lesion of the brain is curable while a tertiary parenchymatous lesion is not; that is to say, in the former the Wassermann reaction in the cerebrospinal fluid rapidly becomes negative, while in the latter it is uninfluenced [7].

This characteristic of "parasyphilis" is constant, and indeed may be said to be diagnostic, so far as the central nervous system is concerned; nevertheless it does not distinguish "parasyphilis" from tertiary interstitial syphilis in other parts of the body, because in certain types of the latter condition treatment is equally ineffective. It is notorious that when the reaction in the serum of a tertiary syphilitic is estimated quantitatively during the course of treatment, the decline in its intensity is usually very slow, or may be entirely absent. In such cases equally with "parasyphilis" it may be argued that treatment is ineffective. This result is the more surprising when it is remembered that the visible lesions, gummata of the skin, rapidly heal after a single dose of salvarsan, and yet the reaction may remain persistent. In our opinion the explanation of this phenomenon depends upon the existence of tertiary syphilitic processes within the body in areas which are anatomically secluded from the effect of an antisiphilitic substance in the blood-stream; thus, although widespread lesions of the skin may be at once resolved, the reaction is still maintained in almost undiminished intensity by hidden foci in other parts of the body.

Such a focus may commonly exist in the aorta. Clinically it is well known that the reaction is most resistant in cases of aneurism and

aortitis, and, moreover, with Turnbull (unpublished) we have found that aortitis is by far the commonest syphilitic lesion in the *post-mortem* room. From this result we conclude that a tertiary syphilitic may commonly suffer from a resistant lesion of the aorta, which will maintain his Wassermann reaction in full intensity in spite of the resolution of other foci. Such a patient would compare with another in whom the Wassermann reaction was maintained by a parenchymatous nerve lesion in spite of the resolution of the interstitial lesion.

On general grounds it might be argued that if one particular area of the body is selected by the *Spirochæta pallida* as a suitable nidus for its vegetation, that area is most likely to be secluded from noxious influences circulating in the blood-stream. In fact, we thought it probable that salvarsan or mercury did not penetrate into the wall of the aorta in sufficient quantity to destroy the spirochætes, and thus that the incurability of aortitis was due to the lack of penetration of the drug. We therefore submitted the organs of certain patients who had died after salvarsan injections to Dr. W. H. Willcox for analysis, and he has found that the aorta contained no arsenic, although other organs were heavily charged therewith (unpublished observations). Such a result supports our view that the persistence of the lesion in the aorta is due to the inability of drugs (and perhaps natural agencies) to reach the spirochætes in the focus.

It will be remembered that in 1911 [21] we were able to announce that, according to the analyses of Dr. Willcox, the brain contained no arsenic after intravenous injections of salvarsan. From this circumstance, which we have since repeatedly confirmed on man and animals, we argued that salvarsan was not fixed by the brain, and was therefore not a neurotropic substance. From continued (unpublished) investigations, however, it is clear that this deduction is incorrect. We have found that if salvarsan is mixed *in vitro* with brain substance, a strong fixation will occur, and thus the absence of arsenic from the brain during life must be due to an inability on the part of this drug to penetrate into the brain. Indeed, if the arsenic does obtain access to the brain, as happens when the drug is inserted into the cerebrospinal fluid, immediate symptoms of toxicity are apparent. As is well known, no arsenic is normally found in the cerebrospinal fluid after intravenous injections of salvarsan; and it is often stated that this is the explanation of the absence of arsenic from the brain. It is supposed that the cerebrospinal fluid functions as a lymph of the brain, and that

substances which enter this organ must do so by way of the choroid plexus and the cerebrospinal fluid. In our opinion, however, this explanation is incorrect. In the course of our investigations we have frequently introduced drugs into the brain substance by the intravenous route, and have never found these drugs to be present in the cerebrospinal fluid. On the other hand, we have met with substances which, like arsenic, will not enter the brain or cerebrospinal fluid, although other organs of the body have contained large quantities. We have, therefore, been led to the conclusion that salvarsan after intravenous injection will not enter the brain substance because of some peculiarity of the cerebral vessels in relation to the drug. The fact that salvarsan is not found in the cerebrospinal fluid has no bearing upon the question.

The effect of these experiments upon the treatment of parenchymatous lesions of the central nervous system is clear. The progress of the lesion cannot be influenced, because drugs cannot penetrate and destroy the spirochætes which are causing this progress. Thus the incurability of "parasymphilis" and of aortitis depends upon the same factor. Similarly the frequent incidence of these two conditions is due to the same cause. When spirochætes succeed in invading the nervous system or aorta in the early stages of syphilis, they have every opportunity for vegetating in these situations until they are thrown into activity at a later date.

Very recently the injection of "salvarsanized serum" into the cerebrospinal fluid has been advocated in the treatment of parenchymatous lesions of the brain. The patient receives an intravenous injection of salvarsan. He is bled one hour later and his serum, diluted and heated, constitutes the therapeutic agent.

The rationale of the method does not appear to be satisfactorily explained. The cerebrospinal fluid is selected as the vehicle because of the prevailing assumption that this is the normal route of entry into the brain, while the "salvarsanized serum" is preferred to the crude drug because it is said to be less toxic and endowed with special therapeutic properties.

We have assisted at the treatment of patients by this method and have failed to observe any obvious justification for it. We have been unable to differentiate the improvement which often follows the initial intravenous dose from the superimposed improvement which is said to arise out of the intrathecal injection.

That the serum has a certain therapeutic effect is probable, since it contains small quantities of salvarsan, but whether these small

quantities of arsenic in the serum have any advantage over an equivalent quantity of crude neosalvarsan is certainly not proved. As shown by Wechselmann, traces of neosalvarsan may be injected intrathecally without harmful results, but when the quantity is increased for the purpose of attaining a more satisfactory therapeutic dose toxic symptoms arise. As in the case of other serous cavities, drugs are rapidly absorbed from the subarachnoid space and can thus directly affect the brain; when neurotropic drugs such as strychnine are administered by this route, in order to obtain the same effect as by other methods it is necessary to diminish the dose considerably. In the case of salvarsan, intravenously injected, the organotropic action is small and therefore the quantity injected may be increased in order to obtain a maximum parasitotropic effect. The conditions are, however, different in the subarachnoid space. Here the drug is highly organotropic, and the "*dosis maxima bene tolerata*" is so small that its parasitotropic effect is trivial.

We are, therefore, of opinion that the intrathecal injection of "salvarsanized serum," or of neosalvarsan in its present form, can have no permanent vogue.

CONCLUSIONS.

The progressive character of "parasyphilitic" lesions is due to a continuation of the syphilitic process in spite of treatment, and not to a progressive primary degeneration of the neurons. The degeneration passively extends to the limits of the neuron, but does not actively spread to other neurons. Treatment is ineffective in resolving the inflammation because drugs in the blood-stream are unable to pass from the capillaries into the nervous substance in order to destroy the spirochætes. If by some method salvarsan succeeds in penetrating into the brain or cord, it produces such toxic symptoms as make its use impossible.

REFERENCES.

- [1] ALTMANN, K., und DREYFUS, G. L. *Münch. med. Wochenschr.*, 1913, S. 464 u. 531.
- [2] BÄUMLER, CHR. "Handb. der spec. Path. u. Therap.," 1874, Bd. iii, S. 36.
- [3] BERGER, H. *Münch. med. Wochenschr.*, 1913, S. 1921.
- [4] CUNTZ, W. "Ueber sogenannte parasyphilitische Affektionen innerer Organe Erwachsener," *Inaug. Diss.*, Heidelberg, 1912.
- [5] EHRLMANN, S. *Deutsch. med. Wochenschr.*, 1906, S. 1115.
- [6] ELLIS, A. W. M. *Journ. Amer. Med. Assoc.*, 1912, vol. lix, p. 1263.
- [7] FILDES, P., and MCINTOSH, J. *Brain*, 1913, vol. xxxvi, p. 193.
- [8] *Idem. Ibid.*, p. 241.
- [9] FORSTER, E., und TOMASZEWSKI, E. *Deutsch. med. Wochenschr.*, 1913, S. 1237.
- [10] FRAENKEL, M. *Zeitschr. f. d. ges. Neurol. u. Psychiat.*, 1912, Bd. xi, S. 1.

- [11] GAUCHER, E., PARIS, et MERLE, P. *Ann. des malad. vénér.*, 1910, t. v, p. 426.
- [12] GRIESINGER, W. *Archiv f. Heilk.*, 1860, Bd. i, S. 51.
- [13] HOFFMANN. *Dermatolog. Zeitschr.*, 1906, Bd. xiii, S. 561.
- [14] HOMÉN, E. A., und LAITINEN, T. *Beiträge zur path. Anat.* (Ziegler), 1899, Bd. xxv, S. 4.
- [15] HUTCHINSON, J. "Constitutional Syphilis," in "System of Medicine" (J. Russell Reynolds), 1866, vol. i, pp. 291 and 301.
- [16] JAKOB, A., und WEYGANDT, W. *Münch. med. Wochenschr.*, 1913, S. 2037.
- [17] LANG, E. *Wien. med. Wochenschr.*, 1880, S. 1305, 1336, 1361 und 1395.
- [18] *Idem.* *Vierteljahresschr. f. Dermatol. und Syphilis*, 1881, S. 469.
- [19] LEVADITI, C., MARIE, A., et BANKOWSKI, J. *Ann. de l'Institut Pasteur*, 1913, t. xxvii, p. 577.
- [20] LEVADITI, C., et ROCHÉ, J. "La Syphilis," Paris, 1909, p. 284.
- [21] MCINTOSH, J., and FILDES, P. "Syphilis from the Modern Standpoint," London, 1911, p. 220.
- [22] *Idem.* *Lancet*, 1913, vol. ii, p. 921.
- [23] MCINTOSH, J., FILDES, P., HEAD, H., and FEARNSIDES, E. G. *Brain*, 1913, vol. xxxvi, p. 1.
- [24] MARIE, A., LEVADITI, C., et BANKOWSKI, J. *Compt. rend. de la Soc. de Biol.*, 1913, t. lxxiv, p. 794.
- [25] MARIE, P., et GUILLAIN, G. *Rev. neurol.*, 1903, t. xi, p. 49.
- [26] MARINESCO, G., et MINEA, J. *Compt. rend. de la Soc. de Biol.*, 1913, t. lxxiv, p. 709.
- [27] NAGEOTTE, J. *Presse méd.*, 1902, p. 1179.
- [28] *Idem.* *Ibid.*, 1903, p. 5.
- [29] NEISSER, A. "Handb. der spec. Path. u. Therap." (Ziemssen), 1882, Bd. xiv (1te Hälfte), S. 682.
- [30] *Idem.* "Beiträge zur Path. u. Therap. der Syphilis," Berlin, 1911, S. 140.
- [31] NICHOLS, H. J., and HOUGH, W. H. *Journ. Amer. Med. Assoc.*, 1913, vol. lx, p. 108.
- [32] NOGUCHI, H. *Journ. of Exper. Med.*, 1911, vol. xiv, p. 557.
- [33] *Idem.* "The Serum Diagnosis of Syphilis." 3rd edit., 1913, p. 167.
- [34] *Idem.* *Münch. med. Wochenschr.*, 1913, S. 737.
- [35] *Idem.* *Journ. Amer. Med. Assoc.*, 1913, vol. lxi, p. 85.
- [36] NOGUCHI, H., and MOORE, J. W. *Journ. of Exper. Med.*, 1913, vol. xvii, p. 232.
- [37] NONNE, M. *Trans. XVII Internat. Cong. of Med.*, London, 1913 (Sect. of Neuropath.), part ii, p. 295.
- [38] ORR, D., and ROWS, R. G. *Brain*, 1904, vol. xxvii, p. 460.
- [39] *Idem.* *Rev. of Neurol. and Psychiat.*, 1906, vol. iv, p. 25.
- [40] *Idem.* *Ibid.*, 1907, vol. v, p. 345.
- [41] *Idem.* *Ibid.*, 1910, vol. viii, p. 721.
- [42] PINARD, M. "L'immunité dans la Syphilis," Paris, 1910.
- [43] PIRQUET, Clemens, Frh. von. "Allergie," Berlin, 1910, S. 60.
- [44] RANKE, O. *Neurolog. Centralbl.*, 1907, Bd. xxvi, S. 157.
- [45] RAVAUT, P. *Bull. et mém. de la Soc. méd. des Hôp. de Paris*, 1903, t. xx, p. 1026.
- [46] RAVAUT, P., et PONSELLE, A. *Bull. et mém. de la Soc. méd. des Hôp. de Paris*, 1906, t. xxiii, p. 3.
- [47] SCHOENBORN, S., und CUNTZ, W. *Deutsch. med. Wochenschr.*, 1913, S. 542.
- [48] SZÉZARY, A., et PAILLARD, H. *Compt. rend. de la Soc. de Biol.*, 1910, t. lxxviii, p. 295.
- [49] STARGARDT. *Biolog. Abt. d. ärztl. Vereins in Hamburg*, 26. November, 1912, *Münch. med. Wochenschr.*, 1913, S. 269.
- [50] STEINER, G. *Deutsch. med. Wochenschr.*, 1913, S. 984.
- [51] STRASMANN. *Deutsch. Zeitschr. f. Nervenheilk.*, 1910, Bd. xl, S. 387.
- [52] UHLENHUTH und MULZER. *Berlin. klin. Wochenschr.*, 1913, S. 2031.
- [53] VERSÉ, M. *Münch. med. Wochenschr.*, 1913, S. 2446.

PUBLICATIONS RECENTLY RECEIVED.

[Notes on a book under this heading do not preclude a subsequent review.]

Archives of Neurology and Psychiatry from the Pathological Laboratory of the London County Asylums. Edited by F. W. MOTT, M.D., F.R.S. Vol. vi, 1914. Pp. 354 numbered consecutively, followed by a series of papers numbered individually. London: P. S. King, 1914.

This volume of these well-known Archives from the Claybury Laboratory opens with a revised version of Dr. Mott's introductory address to the Neurological Section of the International Medical Congress on "The Nature of Parasyphilis." The original report was sent in to the Congress and printed in February, 1913; between that date and the meeting in August, Noguchi discovered the spirochæte in the brain of patients with general paralysis, and other new work necessitated some modification of the original paper. Thus, in the present number of the Archives we have Dr. Mott's reasoned views in the light of modern knowledge. Drs. Candler and Mann follow with "The Wassermann Reaction in the Diagnosis of Mental Disorders" and Dr. Wootton has a short paper on the results of the Wassermann Reaction obtained in Asylum practice. Then comes Dr. Mott's address, given at the opening of the Psychiatric Clinic at Johns Hopkins University, on the "Neuropathic Inheritance, especially in Relation to Insanity." Dr. White gives twenty-five pedigrees of insane persons; Dr. Wootton a number of family histories; Dr. Schuster considers "Hereditary Resemblance in the Fissures of the Cerebral Hemispheres," and Dr. Baines discusses some cases of insanity occurring during the involutional period of life. This is followed by Dr. Fortuny's paper on "Cortical Cell-Lamination of the Hemispheres of some Rodents." The volume concludes with a series of communications by various workers in the Claybury Laboratory to Sections of the Royal Society of Medicine.

Ueber das Sinnesleben des Neugeborenen. Von Dr. SILVIO CANESTRINI, S. 104, mit 60 Figuren im Text und auf 1 Tafel. Berlin: Springer, 1913.

The author of this work attached a tambour to the fontanelle of babies of from 1 to 14 days old; he registered the changes in brain pulsation, associated with various conditions, on a curve together with the respiratory movements. Records were taken from the baby asleep and awake hungry and stilled, and

under the influence of various sense stimuli. Even on the first day after birth light caused a reaction, visible on the curves; some change almost always followed the stronger sounds, although no response occurred to the human voice or to the tuning-fork. As might be expected, gustatory stimuli produced a rapid and profound effect; sugar quieted the pulsations, but sour and bitter solutions produced irregular movements accompanied by cessation of the act of sucking. Olfactory tests caused little or no effect, whilst tactile and painful stimuli either evoked no result or produced the same effect as any state of displeasure.

Das Zittern. Von Dr. JOSEPH PELNAR^Ů, A. o. Professor an der böhmischen Universität in Prag. Aus dem Tschechischen übersetzt von Dr. GUSTAVE MÜHLSTEIN. S. 258, mit 125 Textfiguren. Berlin: Springer, 1913.

When the author of this monograph was assistant to Professor Thomayer, he took graphic records from all patients with tremor whatever its cause. He hoped to be able to make a differential diagnosis by the rate and nature of the oscillations revealed by these curves; unfortunately this was not possible. He deals first with the records he obtained, beginning with physiological tremor and passing through the various intoxications to the neuroses. Then he considers organic nervous diseases such as disseminated sclerosis and Parkinson's disease. Tracings of the tremor in exophthalmic goitre are also given. He then passes on to consider the pathology of these tremors in the light of the literature of the subject and his own observations. This is the weakest part of the book, for he seems to be ignorant of much recent work; thus v. Monakow is not cited and the nucleus ruber is not mentioned.

Traité Clinique et Médico-légal des Troubles Psychiques et Névrosiques Post-Traumatiques. Par R. BENON, Médecin de l'Hospice Générale de Nantes. Pp. 449. Paris: Steinheil, 1913.

A number of excellent cases where a more or less grave neurosis followed injury are reported by the author, who attempts to classify them under the headings of "Dysthénies," "Dysthymies," "Dysphrénies." These correspond roughly to asthenic states, which include chronic mania, affective disturbances, such as anxiety, hypochondria and alterations of character, and lastly, the intellectual affections such as amnesia, Korsakoff's psychosis, confusion and dementia. Unfortunately there is no index, and it is therefore difficult to find the way through this unfamiliar classification; but the cases are admirably described and are well worth perusal. Every chapter is followed by many references to similar instances in the literature, with a short summary of each.

A Manual of Psychology. By G. F. STOUT, M.A., LL.D. Third Edition. Revised and enlarged. Pp. 769. London: University Tutorial Press, 1913.

This well-known work has been almost completely rewritten and revised. It is in fact a new book, and far the best exposition in English of the purely psychological point of view. Everyone interested in the psychical side of his work should study it carefully in order to learn the aspect from which the psychologist looks upon many phenomena with which the neurologist is daily familiar. The book opens with three chapters on the scope, data and methods of psychology and the relation of body and mind. These are followed by a general analysis of the manner in which the conscious subject is related to its objects, with a particularly fine chapter on Attention as the essential form of all mental activity. Book II is devoted to sensation, which, although it suffers from a want of daily familiarity with the facts on which it is based, will act as a useful corrective to loose thinking. Amongst the subsequent chapters of this most interesting text-book we can only mention those on spacial perception, memory, language, ideas and images as particularly important in view of certain materialistic tendencies of neurological thought.

Epidemic Infantile Paralysis. By Professor PAUL H. RÖMER. Translated by H. RIDLEY PRENTICE, M.B. Pp. 208, with 57 illustrations in the text. London: Bale, Sons and Danielsson, 1913.

An excellent translation of the important monograph by Professor Römer on infantile paralysis, noticed in *BRAIN*, vol. xxxiv, p. 536. It contains an account of the fruits of the Nassau epidemic, and a description of the strains of infective material obtained from acute cases of the disease. Everyone interested in the pathology or epidemiology of poliomyelitis should have this book upon his shelves.

General Paresis. By Professor EMIL KRAEPELIN. Authorized English Translation by J. W. MOORE, M.D. (Nervous and Mental Disease Monograph Series, No 14.) Pp. 200. New York: Journal of Nervous and Mental Disease Publishing Company, 1913.

This is a chapter on dementia paralytica from Kraepelin's "Text-book of Psychiatry," translated into English to form a monograph. It gives a good systematic account of the disease as it appears from the point of view of the alienist, but contains little concerning those varieties seen by the neurologist. Kraepelin still holds that "paresis" is a true disease based upon a distinctive pathological process. The translation by Dr. Moore is excellent.

Klinik der Nervenkrankheiten. Von Dr. LEO JACOBSON. S. 488, mit 367 Abbildungen im Text und 4 Tafeln in Farbendruck. Berlin: Hirschwald, 1913.

The best feature of this book is the pictures, which are excellent and almost all original. The text, on the other hand, is commonplace, and contains no information that is not in every text-book of neurology; the subjects in which knowledge has advanced most of recent years are dealt with insufficiently. Localization of lesions in the spinal cord, disease of the brain-stem, optic thalamus, corpus striatum, and cortex cerebri are treated according to the ideas of ten years ago. Evidently the writer is not acquainted with recent French or English work.

Affektstörungen. Von Dr. LUDWIG FRANK. S. 399. Berlin: Springer, 1913.

This work, strongly under the influence of Freud and his followers, is based entirely on the author's patients treated by a combination of hypnosis and psychotherapy. Long and wearisome histories of cases are given revealing the author's naive psychology. There is no index.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I. to XXIII. inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

BRAIN.

PART II., VOL. 37.

THE PHENOMENON OF "TONIC INNERVATION" AND ITS RELATION TO MOTOR APRAXIA.¹

BY S. A. KINNIER WILSON, M.D., B.Sc., F.R.C.P.,

AND

F. M. R. WALSHE, M.D., B.Sc., M.R.C.P.

INTRODUCTION.

PERSONALLY OBSERVED CASES.

CONSIDERATIONS SUGGESTED BY THE ANALYSIS OF OUR CASES.

REVIEW OF ANALOGOUS CASES FROM THE LITERATURE.

TERMINOLOGY AND RELATION TO PERSEVERATION, PROPERLY SO CALLED.

NATURE OF THE PHENOMENON AND RELATION TO APRAXIA.

RELATION TO THE PYRAMIDAL SYSTEM.

RELATION TO MYOTONIA, PROPERLY SO CALLED.

RELATION TO CERTAIN INVOLUNTARY MOVEMENTS.

PATHOGENESIS AND LOCALIZING VALUE.

BIBLIOGRAPHY.

In a paper by Wilson [42] entitled, "A Contribution to the Study of Apraxia," which was published in *BRAIN* in 1908, reference was made to the phenomenon of so-called "tonic perseveration," and a personally observed case was briefly alluded to. The details of that case are here published for the first time. Since that date, we have had the opportunity of studying two further instances of the condition, and this paper is therefore based on an investigation of three cases in which the phenomenon was present in a typical and advanced form, constituting, indeed, the most marked clinical feature. We are greatly indebted to Dr. H. H. Tooth, of the National Hospital, Queen Square, London, under whose care the latter two patients were, for permission to record them. Two of these three patients were successfully operated on for cerebral tumour; hence we are in a position to discuss the localizing

¹ A brief communication on this subject was made before the Neurological Section of the International Congress of Medicine, London, August, 1913.

value of the symptom, which is one of considerable physiological interest.

It must be remarked at the outset that the terminology of the condition is far from satisfactory. No rigorous definition of the expression "tonic perseveration" has hitherto been proposed, but it is understood to signify inability, owing to a central lesion, to relax a given innervation in any muscular group or groups. To give a single illustrative example: Liepmann [27], who coined the term, uses it of his patient the *Regierungsrat*, who was occasionally observed to be unable to let go an object which he held in his left (dyspraxic) hand, grasping it more firmly instead. The innervation of the muscular groups concerned seemed to persist in spite of the patient's endeavour to inhibit it. He could not cut short a muscular contraction once it was begun. Liepmann proposed to denote this type of perseveration "tonic perseveration." We prefer, however, the term "tonic innervation," for reasons which will subsequently appear, as being more accurate and less confusing.

As a matter of fact, however, the terminology not only of this, but of the other two varieties of perseveration distinguished by Liepmann, viz., "clonic perseveration" and "intentional perseveration," is open to obvious objections, which will be mentioned when the matter is discussed in the second half of this paper. It is curious that as far as can be discovered from a careful examination of the passages in his various papers bearing on perseveration Liepmann nowhere makes any allusion to the familiar symptom of myotonus or myotonia in connexion with his "tonic perseveration," nor is the word so much as mentioned by Kleist [23] as far as we have noticed, in his latest contribution to the subject of disturbances of psychomotor function. This appears the more remarkable as, clinically, there is no very obvious difference between the inability to relax a handshake of the patient with myotonia atrophica, that of a patient with Thomsen's disease (myotonia congenita), and that of a patient with "tonic innervation." It is, however, to be clearly understood that in tonic innervation we are supposed to be dealing with a phenomenon of central origin, whatever be the site of the lesion in the other above-mentioned diseases.

This brief allusion, then, to what the term is intended to signify, is simply by way of introduction to our three cases. The many questions of interest suggested by a consideration of them will thereafter be approached.

Case 1.—A. J., male, aged 38, was admitted to the National Hospital under the care of Sir William Gowers on December 16, 1907.

The patient had been married seventeen years: his wife had had three stillborn children, but no miscarriages. He was a right-handed man. He denied venereal disease, but admitted risk.

History of present illness.—In February, 1907, he had an attack of influenza, accompanied by a copious thin discharge from the left ear. About a month later, when playing the piccolo at a public concert, he suddenly felt giddy, began to tremble, and had to stop playing. A few days later, he noticed that he was beginning to drag his left leg as he walked. The onset was quite gradual, and involved the whole of the limb. About one month later, the calf of the left leg used to become cramped as he lay in bed, and involuntary flexor spasms of the limb occurred. About the same time when performing dumb-bell exercises he found he could not make rotatory movements of the left arm easily, and also that he sometimes could not relax his grasp of the dumb-bell in his left hand for a second or two. He noticed the same difficulty in relaxing his fingers when he held a fork in his left hand, also in buttoning and unbuttoning his clothes. There were no cramps in the left arm or hand, and no paræsthesiæ in the limbs. The left arm gradually became weak. For two months prior to admission he had suffered from nausea, without actual vomiting. For a month he had noticed occasional involuntary twitches of the left arm, the limb being abruptly elevated so that the elbow was almost on the same level as the shoulder, while some flexion at the elbow occurred: with these movements some slight twitching of the leg was usually observed. The total duration of these little attacks was a few seconds, and they took place several times a day. During the same month he had been conscious of failing vision, more particularly in the left eye.

State on admission.—The patient was seen to be a heavy, stout, florid man, whose intelligence and attention were good, while his memory was poor. In the right eye the vision was $\frac{6}{6}$, in the left $\frac{6}{12}$. There was advanced double optic neuritis, with 6 dioptries of swelling on the right, and 8 on the left. The pupils were unequal: the right small, irregular in outline, and inactive to light. The left was slightly larger, less irregular, and reacted to light sluggishly. The left pupil moved better on accommodation than the right. There was no ptosis, diplopia, strabismus or nystagmus. The left side of the face was slightly weak in its lower part.

Motor system.—The patient's general muscular development was excellent. There was a certain increase of tonus in the limbs on the left side. There was slight general weakness of the left arm compared with the right, and of the left leg compared with the right, most noticeable in the distal segments. The remarkable feature about the patient's condition was his inability to relax the muscles of the left arm (the phenomenon was less pronounced in the muscles of the leg) after they had been employed in muscular effort. If an object was firmly grasped in the left hand, for a few seconds, the patient was quite unable to relax his grasp, for as long as fifteen seconds, or more, even though he made powerful associated movements with the right hand. If he extended the left arm at the elbow, he was unable to flex it again till some five or eight seconds had elapsed. Direct muscular excitability was not obviously increased.

There was no change in sensibility to the usual tests. The abdominal reflex on the left side was diminished: a double flexor response was obtained. The deep reflexes in the legs were equal: in the arms, the left were brisker than the right.

January 21, 1908.—With the right hand the patient used correctly the following objects: Paper-knife, key, scissors, nail.

Movements on request.

With the right hand:

Turn the handle of a barrel organ.	+
Count out money.	+
Movement of shaving.	+

With the left hand:

Turn the handle of a barrel organ.	Stiff, rather angular rotation movements of whole arm from shoulder.
Smoke a pipe.	+
Button jacket.	Made fair attempt, the fingers being moved very stiffly and slowly.
Put left hand on top of head.	+
Put left forefinger on tip of nose.	+
Put left forefinger into right ear.	Put it into left ear.
Touch tips of left fingers with left thumb.	At first failed because of inability to relax the necessary innervations, but succeeded somewhat better at a second attempt.

With both hands:

Make the movements of playing the flute.	The attitude of the two hands correct: movements of fingers correct on right side, very stiff on left, but approximately correct.
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There was no agraphia or dysgraphia with the right hand. Very good attempts to draw a pipe, a spade, a Union Jack, were made. In writing or drawing with the left hand, it was obvious that the difficulty was entirely due to the patient's inability to move his left arm with any freedom, the fingers and hand frequently became immobilized for some seconds, and he constantly used the right hand to help the other by taking hold of it and moving it about.

February 3, 1908.—The weakness of the left side of the face was now more marked. A special examination was made of the "tonic innervation" phenomenon.

- (1) Strong grasp with left hand for 5 seconds.
- (2) Relaxation took 20 seconds.
- (3) Flexors were then faradized for 20 seconds.
- (4) Then grasp, 5 seconds.
- (5) Again relaxation took 20 seconds.

Interval of 2 minutes.

- (1) The arm was extended strongly for 5 seconds.
- (2) It took 35 seconds for the triceps to relax.
- (3) The triceps was then faradized for 20 seconds.
- (4) Arm extended as before, 5 seconds.
- (5) Relaxation did not occur, in spite of every effort on the part of the patient, for about 38 seconds.

With another trial of the same nature, 105 seconds elapsed before the triceps was relaxed.

On several occasions, when the patient was grasping the fingers of the examiner and was then told to relax, the grasp actually became tighter, and this in spite of the fact that the antagonist extensors were both seen and felt to be contracting in the effort to overcome the tonic innervation of the flexors. The phenomenon was clearly not due to defective innervation of the antagonists of the contracting group.

In the left leg the same feature was present, but in less degree; a succession of quick alternating movements at knee or at ankle was quite impossible because of the difficulty in relaxing a muscle once it had contracted.

The patient's gait was now definitely hemiplegic, but it was noticeable that he was able to move the left leg better when walking than might have been supposed.

The deep reflexes were distinctly brisker on the left side than on the right, there was a tendency to ankle-clonus on the left, and the left plantar response was not so definitely flexor as the right. While the patient was in hospital no movements of the "pseudo-spontaneous" type were ever observed.

February 10, 1908.—The patient was re-examined with regard to the possible effect of massage on the phenomenon of tonic innervation.

- (1) Left hand and arm had been lying at rest for some minutes. Grasp for 5 seconds, strongly.

- (2) This took 8 seconds to relax.
- (3) The extensors of wrist and fingers were then massaged for 2 minutes.
- (4) Grasp, 5 seconds' duration, as before.
- (5) This was instantaneously relaxed.

After an interval of about 2 minutes, the arm was tested again.

- (1) Grasp, 5 seconds.
- (2) This took 10 seconds to relax.
- (3) The extensors of wrist and fingers were massaged for 2 minutes.
- (4) Grasp for 5 seconds, as before.
- (5) This took 15 seconds to relax.

Interval of 5 minutes.

- (1) Grasp, 5 seconds.
- (2) This was relaxed instantaneously and easily.
- (3) Massage to the extensors for 2 minutes.
- (4) Grasp for 5 seconds.
- (5) This took 75 seconds to relax.

The patient was tested again, some hours later.

- (1) Grasp, 5 seconds ; this was relaxed in 5 seconds.
- (2) Grasp, 5 seconds ; this took 10 seconds to relax.
- (3) Massage to extensors, 2 minutes ; grasp, 5 seconds ; relaxation took 40 seconds.

Massage in the following tests was given to the flexors of wrist and fingers.

- (1) Grasp, 5 seconds ; this was relaxed in 10 seconds.
- (2) Massage to flexors ; grasp, 5 seconds ; relaxation, 10 seconds.

The experiment was repeated.

- (1) Grasp, 5 seconds ; relaxation, 10 seconds.
- (2) Massage to flexors for 2 minutes ; grasp, 5 seconds ; relaxation, 2 seconds.

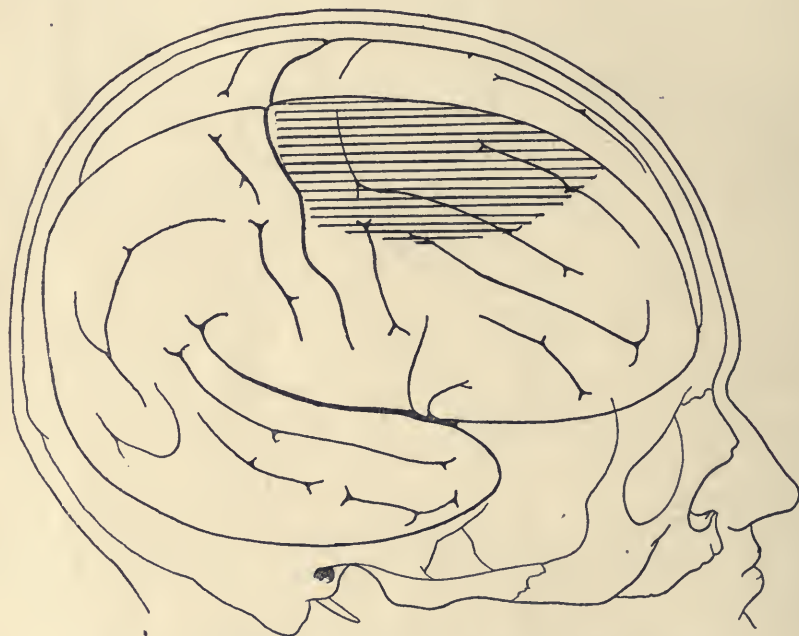


FIG. 1.—Shaded area indicates site of tumour removed in Case 1.

February 11, 1908.—Sir Victor Horsley operated under chloroform, making a large craniectomy over the right frontoparietal region. The dura was seen to be very tense, but not discoloured. It was not opened at this stage. The patient stood the operation very well.

February 18, 1908.—Under chloroform the wound was reopened and the dura incised freely. It was at once seen that the convolutions were much flattened and the brain looked pale. A horizontal incision was made in the posterior end of the superior frontal gyrus ; about $\frac{1}{2}$ in. below the surface a large dark plum-coloured encapsulated mass was discovered. After ligaturing certain

branches of the anterior cerebral artery, the operator explored with his finger round the tumour and was able to remove in its entirety a large endothelioma, encapsulated above but somewhat broken on its under surface, about the size of a tangerine orange. The tumour had extended backwards under the upper third of the precentral gyrus: it extended forwards well into the frontal centrum ovale, and bulged over the midline, pressing on the right side and upper aspect of the genu of the corpus callosum. The lateral ventricle was not opened. The patient stood the operation well.

February 21, 1908.—After the operation there was complete flaccid hemiplegia of the left arm and leg, while the face was less involved. Nevertheless on passive movement at the elbow, flexion and extension alternately, there was always some momentary resistance in the antagonist. This was also found when alternating passive movements were made at the knee. An extensor response was obtained on the left side. The phenomenon of tonic innervation, however, had completely disappeared.

March 24, 1908.—By this date the patient's general health had greatly improved. There was some return of power in the flexors of the left elbow, wrist and fingers, but otherwise the hemiplegia was as before. Slight relative anaesthesia and hypalgesia were present over the left side of the body. An extensor response was obtained on the left and a flexor on the right. There was no reappearance of the tonic innervation.

Five years later (February 11, 1913) the patient reported himself as being in excellent general health, although the hemiplegia was practically unchanged.

Case 2.—W. L., male, aged 47, was admitted to the National Hospital under the care of Dr. H. H. Tooth in May, and again in August, 1912.

The patient had always been a healthy man, was right-handed, and denied venereal disease.

History of present illness.—Twelve months before admission, while he was lying down on a couch at home, his left foot suddenly began to jerk. He was quite conscious and suffered no pain, nor was there any subjective sensation. The jerking spread rapidly up the leg, then appeared at the shoulder and spread down the arm to the hand. The whole fit lasted about ten minutes. Thereafter he noticed that the left arm and leg were weak, and this weakness gradually progressed, though there were no more fits, till for the last four months he dragged the leg very badly when walking. He did not complain of headache, vomiting, or any affection of vision.

State on admission.—The patient was seen to be a well-nourished plethoric-looking individual. His intelligence, memory and attention were good. There was early optic neuritis in both eyes (+4D. R. and L.) with acuity of vision $\frac{6}{6}$ R. and L. The facial lines on the left side were slightly flattened, but the tongue was protruded straight. There was slight spastic paresis of the whole of the left arm, most marked in the distal joints. A similar condition obtained in the left leg. Slight relative hypalgesia and hypæsthesia were present over the left side of the body, including the limbs. The tendon reflexes were brisker on the left than on the right, and an extensor plantar response

was obtained on the left side. The Wassermann reaction in the blood was negative.

The patient remained for about one month in hospital, and went home with his condition unchanged.

Some two months later he was readmitted with an aggravation of symptoms. The weakness on the left side had steadily increased, and in addition he complained of failing vision.

On re-examination the optic neuritis was found to have progressed in both eyes, vision now being $\frac{6}{12}$. There was a minor degree of weakness of the left external rectus. The lower facial weakness on the left side, previously noted, was still present. The hemiparesis of the left limbs was distinctly worse than on the previous admission, and the spasticity had increased in degree. The left arm assumed the typical hemiplegic attitude of flexion and adduction. There was still, however, considerable power and range of movement.

After a stuporose attack on September 5, it was observed that the phenomenon of tonic innervation was present in a striking degree in the left upper limb; it was not noted, however, in the left leg. Owing to the awkwardness with which the patient passed from one movement to another it was difficult to test for apraxia. Such tests as could be performed revealed no definite dyspraxia, hence only a brief selection need here be given.

	RIGHT.	LEFT.
Asked to beckon :	+	Recognizable attempt.
To button his shirt :	+	do.
Shake his fist :	+	Slow but good attempt.
Strike an imaginary match (L hand) on an imaginary box (R hand).		Recognizable attempt.
Sharpen a pencil with knife in L hand.		Instead of moving knife against pencil he moved pencil (R) against knife held immobile L.

Examination of the phenomenon of tonic innervation.—When asked to place his left hand on his head he did so readily. It was allowed to remain there five seconds, and he was then requested to bring it down to his side again. This took no less than three minutes, and even then was not completely accomplished; however, annoyed at his helplessness, he pushed the arm down with his right hand.

(1) Grasp left hand, 5 seconds.

(2) This took no less than $2\frac{1}{2}$ minutes to relax.

Faradization both of flexors and of extensors for 30 seconds made no difference in this relaxation.

Effect of massage.

(1) Grasp, 5 seconds (the extensors having been previously massaged).

(2) Relaxation in 2 seconds.

(3) Grasp repeated one minute later; relaxation without further massage, 35 seconds.

(4) Repeated 10 minutes later, relaxation $2\frac{1}{2}$ minutes.

The flexors having been previously massaged:—

(1) Grasp, 5 seconds.

(2) Relaxation, 5 seconds.

(3) Grasp repeated one minute later; relaxation 5 seconds.

(4) Repeated 10 minutes later; relaxation $2\frac{1}{2}$ minutes.

In endeavouring to relax his grasp it was clear that the patient did try his best to accomplish his object, and understood perfectly what was required. If the examiner attempted to withdraw his fingers rapidly from his hand the grasp of the patient's fingers always tightened perceptibly. On clenching his

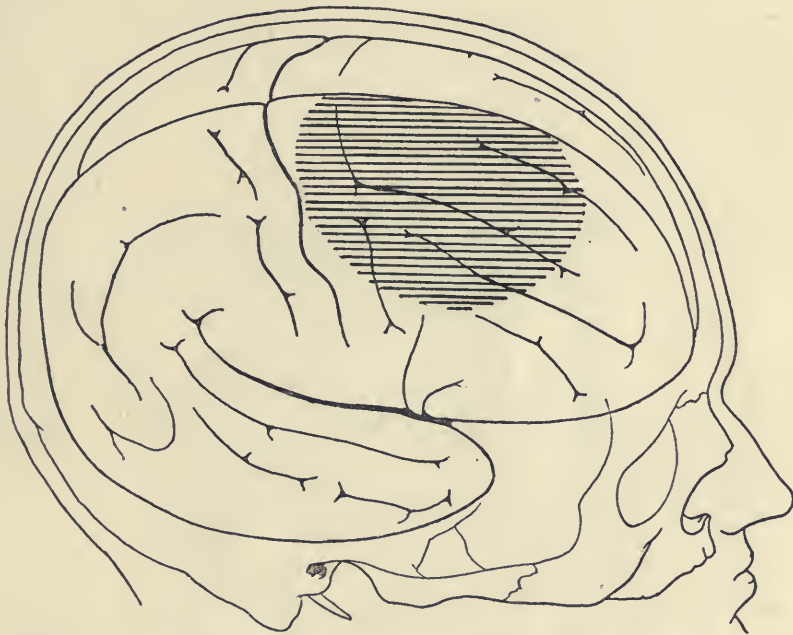


FIG. 2.—Shaded area indicates site of tumour removed in Case 2.

empty fist he seemed to have less difficulty in relaxing—35 seconds usually. He was asked to flex his arm forcibly against resistance, which was maintained for 5 seconds. He was then requested to extend his arm: this took 50 to 60 seconds. During this time the contraction of the biceps slowly died away (as felt by palpation), while the triceps came at once into action and only predominated as the contraction of the biceps passed off.

The completeness of the patient's comprehension of all that he was asked to do was assured by asking him to perform the movements with his right hand, or arm; this he always did readily and easily.

Sensation.—On the left side of the body and left limbs, pain, temperature,

and localization were unimpaired, but there was mild hypæsthesia to cotton-wool, and there was a very moderate diminution in the sense of position. There was no astereognosis.

September 6, 1912.—Right frontal decompression, first stage. Mr. Sargent removed the bone and opened the dura, exposing a plum-coloured tumour situated in the frontal and prefrontal region, as in fig. 2. It was circumscribed and well defined in outline. The patient bore the operation badly.

September 13, 1912.—Second stage: The tumour was exposed and found to be superficial, displacing without actually invading the brain substance. It was removed *in toto*, leaving a bed of depressed cortex. It grew from the falx cerebri by a somewhat pedunculated base, and was of the dimensions of a tangerine orange. It lay exactly over the posterior ends of the first and second right frontal convolutions, extending back to the anterior margin of the fissure of Rolando in its upper part. Its lower border reached $2\frac{1}{2}$ in. laterally from the mid-line. The tumour was an endothelioma.

September 22, 1912.—The hemiplegia became more marked after the operation, for the time being, whereas the phenomenon of tonic innervation completely disappeared.

October 4, 1912.—The patient's general condition was by this date very good. The left upper extremity showed complete paralysis with some spasticity, and the phenomenon of tonic innervation was still quite absent. Eventually a fair recovery was made, and the patient left the hospital in good general health and walking well.

Case 3.—F. F., female, aged 58, was admitted to the National Hospital under the care of Dr. H. H. Tooth on September 5, 1912.

Previous history.—The patient was a right-handed woman who had always enjoyed good health till within a few years of her admission to hospital. For the previous two years or more she had complained of occasional severe "cramps" in the left thigh, and a frequent feeling of numbness and deadness in the left hand, of some minutes' duration. For about the same period of two years the patient had been rather depressed and easily moved to tears.

History of present illness.—On May 15, 1912, she complained of "pins and needles" in the left leg, and by the next morning she had lost the use of the limb. On that day she vomited copiously, and in the course of a few hours the left arm became as "useless" as the leg. There was no loss of consciousness and no headache. Two or three days later she lost all feeling in the left limbs, but this returned in the course of three weeks. Since the onset of the illness there has been a certain amount of mental deterioration; memory has become defective, and the patient has been emotional and unreasonable, and not always, apparently, aware of her failure to control the action of her sphincters. Before admission the left leg improved slightly, but the arm did not. The patient noticed she was unable voluntarily to unclasp the fingers of the left hand, or to let go of things she was holding in the left hand. Occasional brief periods of a degree of dysarthria were noted since the commencement of the illness.

State on admission.—The patient was a healthy-looking florid-complexioned woman, not complaining either of pain or discomfort.

Her attention was not always very good. Her memory for recent events was somewhat defective. During the examination she frequently smiled or laughed for inadequate reasons, and made irrelevant remarks.

Speech.—She comprehended spoken and written speech perfectly. There was no failure in identifying objects and pictures of objects. There was no defect of spoken language. She wrote quite well with the right hand, but there was a tendency, in the first place, to the occasional omission of a letter or a word, and in the second, to a degree of perseveration (in the strict sense of the word, see below). Thus she wrote "God sve th king"; "have yo Pears' soap?" for "have you used Pears' soap?" "Natioal Hospital"; "our Father who art heaven," &c. The perseveration is illustrated by the following: she wrote her name correctly the first time, "Fanny Flynn." The second time she wrote "Fanny Fanny." For "it is a fine day," she wrote "it is a finne day." With the left hand she could do nothing whatever as far as an attempt at writing was concerned.



FIG. 3.—(Case 3.) With the normal right arm patient readily puts finger on nose.

Apraxia and tonic innervation.—As already mentioned, there was a degree of left hemiplegia present. In the case of the left leg there was complete paralysis with contracture. In the arm, however, there was still considerable power present, and no trace of contracture or contraction-attitude. The remarkable feature of the arm condition was, in the first place, the complete motor apraxia. The patient understood perfectly what was required of her, and made no mistakes with her right arm. All the time that the patient was under examination she was seen to move the

left arm freely, and to execute in normal fashion well co-ordinated movements, but only in an automatic way. Thus at one moment she was fingering the bedclothes with the left hand and pulling them up—a favourite occupation—at another, she was scratching her left thigh; then she was seen twisting her wedding-ring, which she wears on her right hand, round her finger with her left forefinger and thumb; in fact, her left arm was practically never still. In striking contrast to this freedom of involuntary movement (a typical example of so-called “pseudo-spontaneous” movement) was her inability to perform any movement with that hand or arm, even the simplest and most elementary, when she was asked to do it, i.e., when on request she consciously endeavoured to use the limb.



FIG. 4.—(Case 3.) With the apraxic left arm patient cannot put finger on nose, and has to grasp the left arm with the right in order to perform the test.

The second remarkable feature of the left arm and hand was the condition of tonic innervation they presented. When the examiner put his fingers into her left hand, her fingers at once closed on his, and she was then unable to relax her grasp. The more he tried to release his fingers the more tightly hers closed round them, until she spontaneously caught hold of his hand with her right and pulled it away from her own left grasp. Once this was accomplished, her left hand relaxed, possibly because she was no longer exercising any conscious volition over it. It was also noticeable that if, while the examiner's hand was still grasped in her left, her attention was successfully diverted, then the examiner could remove his hand more easily. In one of the tests for apraxia a hair-brush was put into her left hand and she was quite unable to let it go when she wanted, and had to make great efforts to pull it away with her right hand.

Some examples may now be given of the phenomena observed during examination:—

Right hand:

Beckoning.	+
Shake fist.	+
Shake hands.	+
Open hand.	+
Close hand.	+
Put hand on head.	+
Touch thumb and little finger.	+
Make movement of cutting with a pair of scissors.	+

With objects in the right hand:

Brush, comb, pipe, button-hook, mirror.	All correctly and readily used.
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It was obvious, in short, that the right limbs were normal in every way.

Left hand.—During examination the left hand was practically never still; the patient usually either held the bedclothes with it, or kept playing with her nightdress with her fingers, or pulled and pushed the bedclothes up and down.

Shake hands.	"I can't quite"; put out three ulnar fingers.
Open your hand.	Repeated the movement of three ulnar fingers.
Close your hand.	Opened it, then caught hold of the bedclothes and pulled them up; "I can't."
Put hand on head.	"I can't, sir"; all the time she moved her hand about at her neck and chin in an aimless way. "It's too heavy"; then seized it with the right hand and tried to put it on to her head.
Touch thumb and each of fingers in succession.	"I can't, sir"; put thumb in between third and fourth fingers and kept it there.
Shake fist.	A fair attempt.
Beckoning.	"Isn't it funny I can't do it? It is certainly very extraordinary." Opened hand and simply looked at it.
Cut with pair of scissors (no object).	Repeated exactly what she did for "beckon."

Tested with objects in the left hand:

Brush.	This was put into her left hand; she grasped it firmly, turned it round and round, did nothing else, and was incapable of letting it go. The brush had to be pulled away by main force. The brush was put into hand again, and then she was invited to "let it drop." Of this she was absolutely incapable. She kept twisting and turning
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- it round and round, moving her fingers over it. A moment before, she had opened her hand merely by looking at it, and it was frequently the case that the examiner could get her to relax her grasp by saying *suddenly*, "Look at your hand," when she automatically opened it and looked at her palm. She was not told to *open* her hand, but merely to *look* at it.
- Comb. Holding the comb firmly in an awkward way, she put it into her mouth, and made an irregular movement as though to comb to and fro. Knew quite well that this was wrong, and said so.
- Button-hook. Did nothing with it. Said it was a button-hook, then made wild endeavours to get it out of her left hand and transfer it to the right.
- Mirror. Held it reversed, but managed to turn left forearm round so as to look into the glass, and was able (on this occasion) to let it drop from her hand.
- Bilateral movements:*
- Put out tongue. Correct. Kept tongue protruded as though she had forgotten it was out.
- Shut your eyes. "I can't do it": shut them for a single moment only. "You've done it." "Have I? I can't do it." Could not in any way manage to keep them closed for longer. The closure seemed more involuntary than otherwise. Could always close them if an object was approached to them.
- Whistle. Fair attempt, after a failure:
- Cough.
- Wrinkle forehead.
- Frown: blow out cheeks.
- Sigh.
- Take a deep breath.
- Make movements of playing the piano. Right correct, left simply nil.
- Put your hands as in prayer. Right instantly put up to correct position, while the left remained entangled in the coverlet of the bed.
- Tie a knot in a piece of string (given). By using her teeth and her right hand mainly she managed to accomplish this. Her left fingers caught in the string and she could not get them out.
- Open a pencil-holder (given). Managed this also, using the right hand almost entirely. She could not get the end of the holder out of her left hand. "Isn't it tiresome?"

The next moment she had grasped the clothes with her left hand and pulled them up to her chest.

Strike a match on box (given). She moved the box up and down in an ineffective way against the match head, held in left hand. When the examiner had pulled the match out of the patient's left hand, she suddenly put her left hand up with the greatest readiness and wiped the point of her nose with it.

October 10, 1912.—Both apraxia and tonic innervation were unchanged. The patient's memory was much as before; however, she seemed to be remembering incidents of her hospital life very well. Her attention was still easily distracted. Orientation in time and space was much improved from the time of her admission. There were neither hallucinations nor delusions. Her habits were still faulty, i.e., her control over her sphincters seemed impaired.



FIG. 5.—(Case 3.) In a bilateral test ("hands as in prayer"), normal right arm and hand; left hand and arm, apraxia and tonic innervation (patient cannot let go the bedclothes).

The patient's faculty of imitation of movements was examined. The hands of the observer were placed together in the attitude of prayer, the patient having been previously asked to imitate the movement. Her right hand was immediately placed in the middle line of the body in the desired attitude, while the left hand was slowly and imperfectly brought into a position more or less analogous, the patient having great difficulty in releasing the bedclothes which she was grasping with her left hand. Sometimes she brought the hand up and the bedclothes along with it. It frequently happened that the patient



FIG. 6.—(Case 3). Patient endeavours with her right hand to pull a small object out of the left hand which grasps it firmly. Note innervation of the left extensors in the endeavour to overcome the tonic innervation of the left flexors.



FIG. 7.—(Case 3.) Patient is unable to relax the tonic innervation of her left flexors.

imitated with her right hand the movements that the examiner was making with his left; often only a very feeble attempt was made with the left, apart from the tonic innervation of the limb.

The performance of single movements with the left hand, on request, was as imperfect as on the patient's admission. Movements of expression, such as "throw me a kiss," were correctly performed on the right side; on the left



FIG. 8.—(Case 3.) The more patient tries to inhibit the tonic innervation, the firmer does her grasp become, so that the observer is able to pull her arm right over to the other side.

the hand was very slowly and imperfectly approximated to the lips; the head was bent forward to meet the hand, which remained stiffly in position although the patient then withdrew her head. The tonic innervation remained unchanged.

Examination of rest of nervous system.—No defect of cranial nerves beyond slight weakness of the muscles of the left side of the face was present. The ocular movements were free; there was no nystagmus. The optic discs were normal, the pupils were regular and equal, and their reactions normal. There was definite though slight general weakness of the left arm, and to a greater extent of the left leg. There was some spasticity of the left arm, apart from

the tonic innervation, and more in the leg, which was in a state of contracture.

Examination of the sensory system was difficult because of the patient's failure to attend properly. Apparently there was slight diminution of cutaneous sensory acuity in the peripheral part of the left arm. Muscular sense was probably somewhat diminished distally. At one time it appeared that the patient was not always able to recognize by touch objects held in the left hand, but this condition varied and was not constant. There was no ataxia of the left arm.

The tendon reflexes on the left side were brisker than on the right; there was ankle clonus on both sides, left greater than right, and a plantar extensor was always obtained on the left side, probably a flexor on the right. The Wassermann reaction in the blood was negative.

Before the patient left hospital (December 14, 1912) it was noted that with the eyes closed her control over the movements of the left side was extremely poor. The apraxia and tonic innervation, especially the former, seemed worse when the eyes were closed; if they were open the apraxia improved although she was not actually looking at the way in which the arm was moving.

If, now, we summarize succinctly these three cases, their chief features may be described as follows:—

In Case 1 a male patient, aged 38, gradually developed weakness of the left leg and later of the left arm, and simultaneously with the latter he found that he was unable to relax the muscles of the left arm readily after they had contracted in any voluntary act. During the same time occasional little attacks of involuntary twitching of the musculature of the left arm occurred. Occasionally, also, cramps and involuntary spasmodic movements of the left leg took place, mostly as the patient lay in bed. On examination he presented characteristic signs of cerebral tumour, with headache, nausea, and advanced double optic neuritis. The muscles of the left face and limbs were weaker than those of the right, and there was distinct increase of tonus in them. The left abdominal reflex was diminished, and the tendon reflexes on that side were increased, but there was a double flexor response. No alteration in sensibility could be detected, and there was no ataxia. In the left arm, and to a less extent in the left leg, the phenomenon of tonic innervation was present in a striking degree. If an object was grasped in the left hand the patient was unable to relax the innervation for a full minute or more, although he made powerful associated movements with the right arm, and although the tendons of the antagonist group could be seen distinctly to contract. Frequently the grasp became tighter the more he endeavoured to inhibit it. Other muscular groups,

both flexor and extensor, showed the same phenomenon. The right arm was entirely normal. There was no apraxia or dyspraxia of the left arm, but the defect of innervation hindered the patient in carrying out requests. There were no involuntary movements of the "pseudo-spontaneous" type. Fair attempts at writing were made with the left hand. The left limbs gradually became more hemiplegic, and ankle-clonus developed. The patient was successfully operated on, and a large endothelioma removed from the right hemisphere. It lay immediately underneath the posterior end of the right superior frontal gyrus, extending backward under the upper third of the precentral gyrus and forward into the centrum semi-ovale. It bulged on the mesial aspect of the hemisphere and impinged on the right side and upper aspect of the anterior half of the corpus callosum. After the operation the tonic innervation completely disappeared and a typical hemiplegia of moderate degree, with characteristic reflexes, remained.

In Case 2, a male patient, aged 47, developed a characteristic but not severe Jacksonian attack of the left limbs, beginning in the foot and passing rapidly up to the shoulder, then down the arm to the hand. Gradually progressing weakness of the left limbs followed, the leg being more affected than the arm. At this time, on examination, there was found to be slight double optic neuritis, slight spastic paresis of the left limbs, including the face, and slight relative hypæsthesia on the left side. The tendon reflexes on the left were increased, and an extensor response was obtained. Two months later the weakness on the left side had increased, and the left arm assumed the contraction-attitude of an ordinary hemiplegia. There was, nevertheless, no great loss of strength in it. It was now observed that the phenomenon of tonic innervation was strikingly present in the left upper limb, both in flexor and extensor groups. When the patient put his left hand on his head he was unable to bring the arm down for three minutes, owing to tonic innervation of the muscular groups concerned. The right arm was entirely normal. There was no apraxia or dyspraxia in the left hand, but the tonic innervation interfered with his passing readily from one movement to another. There were no "pseudo-spontaneous" movements, and no ataxia. Fair attempts at writing were made with the left hand. The patient was successfully operated on, and a large endothelioma was removed from the right frontal lobe. It pressed deeply into, but did not invade the cortex. It grew from the falx, and lay exactly over the posterior ends of the right superior and middle frontal gyri, extending to the anterior margin of the fissure of Rolando.

After the operation the phenomenon of tonic innervation entirely disappeared, and a typical slight spastic hemiplegia remained, with characteristic reflexes. Eventually a good recovery was made.

In Case 3, a female patient, aged 58, had suffered for two years from indefinite attacks of cramp in the left thigh and from paræsthesiæ in the left hand. Four months before admission to hospital she had an attack, without loss of consciousness, in which the left arm and leg became powerless, and all feeling left them. Improvement set in, however. It was thereafter noted by the patient that she was unable to relax her grasp easily on the left side, and unable to relax other movements of these limbs. On admission she was found to be rather emotional and inattentive. There was no trace either of motor or of sensory aphasia. She wrote quite well with the right hand. On the left side there was a spastic hemiparesis, the leg being much more involved than the arm, in which considerable power and freedom of movement were still present. The chief motor phenomena were as follows—all confined to the left limbs (arm):—

(1) Severe motor apraxia; complete inability to perform movements to order which she performed automatically without any difficulty; no ideational apraxia, and no ataxia.

(2) Constant “pseudo-spontaneous” and “amorphous” movements.

(3) Inability to imitate movements.

(4) Tonic innervation.

(5) Agraphia.

Apart from the tonic innervation there was some spasticity of the left arm. The reflexes were brisker on the left side than the right, and on the former an extensor response was always present. The condition of sensibility was a little difficult to determine; apparently there was diminution of cutaneous sensibility in the left limbs; there seemed to be impairment of the muscular sense. Stereognosis also appeared to vary. The patient eventually left the hospital practically *in statu quo*.

CONSIDERATIONS SUGGESTED BY THE ANALYSIS OF OUR PERSONALLY OBSERVED CASES.

Before going on to a detailed investigation of the phenomenon of tonic innervation we may here indicate several important considerations suggested by the examination of these cases, which will aid subsequently in coming to our conclusions as to the significance of the symptom.

(1) In the first place, it is clear that tonic innervation may occur by itself, i.e., without either dyspraxia or apraxia. Our first two cases exemplify this well. The two conditions are not causally connected; one is not the inevitable accompaniment of the other. Where the two occur together, therefore, it is possible to separate the mechanisms clinically.

(2) Our first two cases serve to determine the localizing value of the phenomenon; in each case the tumour lay in practically the same position. It will be readily understood that the combination of tonic innervation and of motor apraxia is not unexpected, inasmuch as the site of the lesion in the uncomplicated cases is in the immediate neighbourhood of one of the sites whence motor apraxia may be derived, and our third case shows this.

(3) In all our cases tonic innervation was present in association with slight but unmistakeable involvement of the cortico-spinal path; in each there was slight spasticity of the affected limbs, and characteristic alterations in the cutaneous and deep reflexes were present. At the same time, it should be noted that the greater the involvement of cortico-spinal fibres, the less marked was the tonic innervation. In each case the leg was more severely affected than the arm and the phenomenon was there less in evidence. Where the paralysis was profound the phenomenon was absent. After the operations in the first two cases, the tonic innervation disappeared with the development of a post-operative hemiplegia.

(4) The symptom was evident solely and exclusively during voluntary innervation of the muscular groups concerned. In Case 3, for instance, the patient might automatically put up her hand to rub the point of her nose and do so with the greatest readiness, but the effort to do so with full voluntary intent always resulted in a persistent tonic innervation which effectually inhibited the attainment of the desired end.

(5) The symptom is not necessarily accompanied with, still less derived from, any constant sensory changes in the affected limb or limbs.

(6) In all our cases it was strictly unilateral, and is, therefore, localizable.

(7) We were not able to satisfy ourselves that either electricity or massage had any constant effect in curtailing the duration of the tonic innervation. It may be remarked, also, that the electrical changes described as the myotonic or neuromyotonic reaction were not present in our cases in characteristic form.

REVIEW OF ANALOGOUS CASES FROM THE LITERATURE.

Hitherto, as far as we are aware, no article has appeared expressly devoted to a consideration of the symptom of tonic innervation, hence it has been a matter of some difficulty to collect cases in which reference to it has been made, and it may be that others, of equal importance, have escaped our notice. We have been able, however, to collate not a few instances of the occurrence of the symptom in association with intracranial disease, and these will now be enumerated.

(1) Liepmann's [26] patient was frequently unable to relax a given innervation of the left upper extremity, which, be it remembered, was not apraxic, or showed only slight dyspraxia. His wife noticed that when he grasped an object in the left hand he was often unable to let it go from his hand, but held it in a tonic cramp. The symptom, however, was apparently neither constant nor notably developed, and the author's references to it are few and not prominent. A complete left hemiplegia, which occurred not long before the patient's death, complicated matters and made further investigation impossible. At the time when the tonic innervation was observed there was slight weakness of the left half of the face and to a less extent of the arm.

(2) Steinert's [39] case (his Case 2) was that of a man, aged 36, with typical signs of intracranial tumour. There was gradual onset of weakness of the right limbs, the leg being more affected than the arm, with slight spasticity of the same. When at rest, they assumed the attitude of hemiplegia to some extent. No sensory changes were noted; the right abdominal reflex was absent and a right extensor response was present. The patient held fast anything he grasped with the right hand, unable to loosen his hold. He had great difficulty in relaxing a handshake. Only with great effort could the examiner release his fingers from the grip of the patient's right hand. There was no apraxia or dyspraxia in either hand, apparently; at least it is not specifically referred to.

The lesion was a glioma involving the mesial aspect of the left hemisphere, destroying the left gyrus fornicatus and invading the corpus callosum from genu almost to splenium; it compressed the gyrus calloso-marginalis, the paracentral lobule, and the internal capsule, and it bulged across the middle line, towards the corresponding gyri of the mesial aspect of the right hemisphere.

(3) In Steinert's experience the symptom is rare; he had only seen it in one other case, to which brief allusion is made. The patient was a male hemiplegic, who was able to extend his paretic arm at the

elbow; his flexors were weak, but even passive flexion at the elbow was thereafter for a short time impossible owing to tonic innervation of the triceps, and that in spite of every endeavour of the patient to relax. The condition gradually disappeared as the patient improved.

Reference is made to it here, although the details are rather meagre.

(4) Van Vleuten's [41] case is mentioned in Wilson's paper on apraxia referred to above. The patient was a man, aged 55, whose symptoms began with difficulty in finding words—slight amnesic aphasia and verbal paraphasia. There was some weakness of the right side of the face, while definite symptoms of involvement of the right limbs, in the shape of weakness or alteration in the reflexes, were at this stage absent. On the right side, nevertheless, two symptoms occurred; viz., moderate tremor of the right arm when at rest, increasing with muscular exertion, and characteristic tonic innervation of the same. If the patient took an object in his right hand he was unable to let it go, in spite of every endeavour and the urging of the examiner; other muscular groups showed the same tonic innervation, and it was present also in the right leg, to a less extent. The tonic innervation mechanically interfered with the performance of movements of the right limb, but there was no apraxia. On the other hand, however, definite motor apraxia was noted in the left arm and hand. The condition steadily progressed, till eventually the patient sank into a state of apathy and stupor. By this time a right hemiplegia had developed and the tonic innervation disappeared; on the left side the apraxia was more complete.

The lesion was a tumour of the left frontal centrum semi-ovale, destroying the white matter underneath the left cingulum and limbic lobe, as well as that of the superior frontal gyrus; it invaded the left side of the corpus callosum from the genu backwards almost to the splenium, and also grew to some extent into the left lateral ventricle. The basal ganglia and internal capsule and gyri centrales were intact, but pressed on somewhat and distorted a little by the pressure.

(5) Kleist [20] has published a very full record of a case on which he bases his conception of "cortical or innervation-apraxia." The patient was a man, aged 44, with a syphilitic history. He developed a left hemiplegia, then later an incomplete right hemiplegia, with difficulty in speaking. On examination there was found to be a moderately severe degree of motor aphasia, with bilateral spasticity of the limbs, increased deep reflexes, and bilateral ankle-clonus. From their hyper-tonicity the limbs offered considerable resistance to passive movements,

the rigidity resembling that of paralysis agitans, i.e., involving both flexor and extensor groups. The disturbances of motility exhibited by the patient were of great interest, consisting in a form of motor apraxia more pronounced on the right side than on the left. It frequently happened that in attempting to carry out a given movement the patient innervated the wrong group of muscles, and made other mistakes referable to the complexity of the innervation required, which do not concern us further here. In addition, the phenomenon of tonic innervation was present in a well-marked form. When it was desired either to end a given innervation, or to replace it by another, the patient was unable to do so. In dealing cards, for instance, he had the utmost difficulty in opening his closed fingers. In his use of a hammer, the phenomenon was particularly well exemplified. Instead of bringing the hammer down smartly on to the object, tonic innervation and extremely slow relaxation of the muscles that lift and extend the arm resulted in the hammer descending with amusing gentleness. Tonic innervation also occurred in writing.

The symptoms in this case were asymmetrically bilateral. On the left side the slowness of movement, tonic innervation, and difficulty in executing fine movements were more marked, while substitution-movements were better seen on the right. The apraxia of the left upper extremity, in other words, closely resembled what occurs in the limb-kinetic type, and was analogous to cortical hemiplegias or monoplegias with loss of fine movements, while the right-sided apraxia came rather into the category of transcortical motor apraxia (of Heilbronner: Liepmann's ideokinetic apraxia, or motor apraxia *par excellence*). The case was purely clinical, but Kleist postulated lesions more or less resembling those found in Liepmann's case; he thought the left-sided dyspraxia could be explained by a lesion in the left hemisphere; in addition, there must have been a lesion "in or in the immediate neighbourhood of the right central gyri or their underlying white matter." No attempt is made to correlate any of the postulated lesions with the symptom of tonic innervation.

Another case of a differing type, recorded by the same author, will be mentioned later.

(6) A good case has been put on record by Kurt Goldstein [12] [13]. To it our Case 3 bears an altogether extraordinary resemblance.

The patient was a woman, aged 57, who had a stroke on the left side. The left leg remained badly paralysed, while the condition of the face and arm cleared up to a large extent. The following phenomena, however, remained, and concerned the left side only:—

(a) Severe motor apraxia; there was great difficulty in the performance of movements voluntarily which were accomplished automatically with ease.

(b) Frequent "pseudo-spontaneous" and "amorphous" movements.

(c) Poverty of spontaneous movements and marked impairment of "movement-intention." When the patient made any voluntary movement correctly to order, she regarded her success as accidental. There was no "will-feeling" in her spontaneous acts.

(d) Inability to imitate movements.

(e) Tonic innervation in many movements of the left side.

(f) Agraphia.

There was slight cutaneous hypæsthesia on the left side, with considerable diminution of pressure-pain, as well as of the sense of movement and of passive position. Localization, too, was defective. The tendon reflexes were increased on the left, and the plantar response was doubtful. Her left hand was constantly catching hold of the bedclothes in pseudo-spontaneous fashion. When objects were grasped in her left hand she was unable to let them go. Once she thus caught hold of her neck and "nearly strangled herself." She opened her mouth readily when eating, but could scarcely do it on request, and so on. There was no ataxia. The patient was "incontinent" of urine and fæces, but this was probably apraxic in origin; she would sit on the commode for an hour without any result, then was "incontinent" as soon as she was put back to bed.

In almost all its details this case shows a remarkable similarity to our third case, hence the value of the pathological findings is enhanced.

The lesion was a large softening in the distribution of the posterior branch of the right anterior cerebral artery—the branch to the corpus callosum. The softening extended along the mesial aspect of the right hemisphere, destroying the gyrus fornicatus and its white matter, the posterior extremity of the superior frontal gyrus, part of the cortex and white matter of the paracentral lobule, as well as the right hemisphere part of the corpus callosum in almost its whole extent. The central gyri, otherwise, and the internal capsule and basal ganglia, were untouched.

(7) In Kroll's [24] paper there is a case (his Case 3) which has some bearing on our subject. The patient was a man, aged 45, in whom gradual weakness, first of the right side and then of the left, developed. On examination there was slight motor and sensory aphasia,

slight right hemiplegia, with increased tendon reflexes and moderate spasticity. Sensibility was normal. The patient was absolutely blind. There was very definite motor apraxia of the right limbs, and also to some extent of the left. Tests for bilateral movements brought out the apraxia very well. He made all sorts of "pseudo-spontaneous" movements with the left hand, but was incapable of accomplishing any correctly on request. Imitation of movements passively impressed on either side was impossible. According to Kroll the patient also showed constant evidence of Liepmann's "tonic perseveration," apparently with both right and left limbs, but it is not certain that the author is describing the phenomenon with which we are here concerned. Thus the patient frequently held a limb, after moving it, in a given position for a considerable time, but it is not clear whether he simultaneously endeavoured voluntarily to relax the innervation and failed to do so. "In all his movements the patient evinced a tendency to maintain any given pose of his limbs once it was assumed, e.g., he held his fingers for a long time spread out." Kroll calls this "tonic perseveration," but in the absence of details as to the muscular condition, one may take leave to be dubious, the more so as it is stated that "the at first strongly marked apraxia gradually changed into a practically constant state of tonic perseveration." The condition, in our opinion, appears rather to have been analogous to the "Willenlosigkeit" of some of Pick's patients (see below), where movement came to a standstill altogether.

The lesions were softenings in the left middle frontal gyrus, in the left supramarginal gyrus, and in both right and left angular gyri, involving the optic radiations. In addition, the whole of the right hemisphere part of the corpus callosum was disintegrated.

(8) A similar uncertainty exists in regard to a case reported by Coriat [7] (his Case 1). The patient was a young man, aged 24, with symptoms of intracranial tumour. There had been transient paralysis of the left limbs, in which there was considerable defect of cutaneous sensibility. On examination of the patient's motility it was found that typical motor apraxia of the left arm and hand existed, while the right side was normal. There was no ataxia. "In spite of the . . . slight weakness and spasticity of the left arm, he could spontaneously lift it above his head, flex, extend, pronate, supinate, fairly well extend and flex the fingers and give a fair grasp, although there was a disinclination on the part of the subject to use this left arm spontaneously." It is doubtful whether the author is employing the term under discussion

in the sense accepted by German authorities and by us when he goes on to say, "This tendency to akinesia was probably due partly to the patient's appreciation of his localized motor apraxia, and partly to a state of tonic perseveration." And to exemplify the latter, he adds: "The left-sided apraxia became more marked when the patient's eyes were closed. . . . A key, a match, and a drinking glass were used correctly with the right hand and decidedly awkwardly and fumblingly with the left. When attempts were made to use these same objects with the eyes closed the left hand seemed to become petrified, as it were, after an abortive start. In other words we seem to have here the phenomenon of tonic perseveration." "Sometimes the subject becomes petrified, as it were, in the attitude of executing a simple or complex act either requested or spontaneous; this is known as tonic perseveration."

We are of the opinion that in this instance also the condition is that where voluntary action comes to a standstill, a condition to be sharply differentiated from tonic innervation.

(9) Rhein's [35] case was unfortunately even more than usually complicated; nevertheless, his patient exhibited true tonic innervation in the left arm and hand.

The case was that of a man, aged 55, who when he came under observation was quite blind; he had complete loss of the sense of position, could not localize any cutaneous stimulus, and did not appreciate touch or painful stimuli in the left arm. There was also complete astereognosis. There was no paralysis, but the left arm was rarely if ever moved voluntarily. The right arm was apraxic; with the left he was frequently seen to make automatic or reflex movements correctly enough. "When asked to grasp the hand of the examiner with his left hand he occasionally succeeded, and at such times he would not relax his hold, apparently involuntarily in fact, grasping more and more tightly as long as the hand of the examiner remained within his grasp. This was undoubtedly a manifestation of perseveration, of the tonic variety described by Liepmann." No ataxia was observed. The left limbs were rather more spastic than the right; the deep reflexes were increased, and there was no extensor response.

"The autopsy revealed the presence of degeneration of the white matter of the right occipital and parietal regions, on the convexity, and the posterior portion of the temporal lobe. . . . On the left side there was degeneration in the occipital and temporal regions to a much less degree. . . . The corpus callosum, in its posterior portion, was degenerated. . . ."

Rhein quotes Liepmann's view that tonic perseveration is due to disturbance of the motorium itself, and considers this opinion confirmed "somewhat" by the pathological findings in his case, in which the right postcentral gyrus was in part degenerated: "that is, provided we believe that the motor centres are not entirely confined to the pre-central region." But Rhein himself also states, in his description of the autopsy, that "the inner surface of the dura was covered with a thick plastic exudate, *extending over the entire surface of the brain on the right side*, an intense internal pachymeningitis" (italics ours). Evidently this pathological condition ought not to be ignored in a consideration of the clinical import of the lesions. In any case, the profound sensory changes in the left arm (as elsewhere) complicate the purity of the symptom.

(10) An interesting case of agraphia from frontal tumour has been published by Macfie Campbell [6]. The patient was a woman aged 55, with general symptoms of increased intracranial pressure. She showed a writing defect which was not explained by the presence of either a motor or a sensory aphasia. There was no apraxia. Dysarthria was present, and there was some weakness of the right side of the face, and of the right limbs. It was noticed that there was a tendency to (true) perseveration, for instance in answers to questions; and in addition "the motor condition of the right hand was interesting; when the strength was tested at first slight weakness was observed, but in a little while the grip seemed nearly as strong as that of the left hand; when told to let go, the patient did not at once relax, but required to be urged to let go." And again: "After admission to the hospital there was noticed the same tendency to motor perseveration and also *inability to relax promptly* as well as a want of spontaneous utilization of the arm, without there being any reduction in the muscular force of the arm when innervated" (italics our own).

Although the details would have been more valuable to us had they been more specifically dealt with, it is possible to claim this case as one of tonic innervation of certain groups in the right arm.

The lesion was a large cyst of the left frontal lobe, separating the superior and middle frontal gyri; its posterior limit corresponded with the central fissure. The mesial aspect of the left hemisphere bulged inwards and downwards, and there was a corresponding depression of the opposite hemisphere.

(11) In Pick's [33] "Studien über motorische Apraxie" some cases are described which have a bearing on the problem before us.

One of his patients (case Prokop), asked to lie down on his bed, lay down with his right leg stretched in an awkward position over the edge; it was held so, immobile, for more than two minutes. The same patient, asked to take a drink out of a jug on the table, went and put his lips and face into the mouth of the jug and remained so practically without moving. Another patient (case Havranek), asked to light a candle, held the match alight in her right hand, in the neighbourhood of wick, quite immobile, until the match actually burned her fingers.

These incidents are quoted because they exemplify persistence of a given innervation-complex, but at the same time they must be differentiated from the phenomenon of tonic innervation, to which the resemblance is but superficial. The persistence of an attitude, the akinesia following on movement, is not maintained *in spite of* the patient's every endeavour to inhibit the innervation, but from a defect on a higher plane, a "will-lessness" which is not identical with inability to execute the behests of a normal "will" as in tonic innervation.

(12) A case which has been published by Kleist [21] under the title of "Nachdauernde Muskelkontraktionen" may finally be alluded to.

The patient was a woman, aged 29, who from about the age of 16 had suffered from a certain awkwardness of hand movements, and noticed she could not relax her grasp properly. In addition there were weakness and undue fatigability of many of her muscles. On voluntary contraction of the small muscles of the hands, flexors and extensors of fingers, biceps, triceps, pterygoids, peroneus longus and brevis, &c., they passed into a condition of myotonia. As a rule, the more successive identical movements were made, the worse the myotonus; in this respect, therefore, the case differed from the classical myotonia congenita. Certain muscle groups, including the sternomastoids, the dorsiflexors of the feet and the extensors of the arms and the abdominal muscles were atrophic. In addition, kypho-scoliosis, pes equinus and claw-foot, slight peripheral contractures in the arms, paresis of the lower face, slight bilateral ptosis, slight sensory changes and vasomotor disturbances were noted.

The exact nature of the case is not clear. The author considers it an atypical myotonia: Batten and Gibb [1] include it, under reserve, as a case of myotonia atrophica, while Bramwell and Addis [3] place it definitely in their group A, comprising forty-five recorded cases of myotonia atrophica resembling each other more or less closely in the matter of the distribution of the atrophy.

TABLE OF REPORTED CASES OF TONIC INNERVATION.

No.	Author	M. or F.	Side affected	Pyramidal affection	Apraxia	Nature of lesion	Site of lesion
1	Goldstein...	F.	Left arm	Slight weakness of left arm, much more of leg	Left motor apraxia	Vascular	Softening of right superior frontal gyrus, gyrus fornicatus, white matter of paracentral lobule, and whole of right side of corpus callosum.
2	Kleist ...	M.	Left limbs chiefly	Some left hemiplegia, also right	Left limb-kinetic apraxia, right motor apraxia	Syphilitic	(Clinical case.)
3	Liepmann	M.	Left arm (occasional)	Slight weakness left face and arm	Gross apraxia right, slight dyspraxia left	Vascular	Widespread softening: left frontal and parietal, corpus callosum, right internal capsule.
4	Rhein ...	M.	Left arm	Slight spasticity of left limbs	Right apraxia, left (?) (case complicated by gross sensory loss)	Pachymeningitis	"Over entire surface of brain on right side," &c.
5	Steinert ...	M.	Right arm	Progressive right hemiplegia	?	Tumour	Left mesial gyri anteriorly, corpus callosum; left paracentral lobule and internal capsule pressed on.
6	van Vleuten	M.	Right arm, slight in right leg	" "	No apraxia right, definite motor apraxia left	"	Left frontal semi-ovale, white matter under superior frontal and mesial gyri, left side of corpus callosum; left internal capsule pressed on.
7	Wilson and Walshe	M.	Left arm	Slight affection of left arm, much more of leg	None	"	Posterior end right superior frontal gyrus, under mesial gyri, at corresponding level, pressing on upper precentral gyrus and right corpus callosum.
8	" "	M.	"	Slight spastic paresis left arm, more of leg	None	"	Pressing into posterior ends of right upper and middle frontal gyri, extending to anterior margin of fissure of Rolando.
9	" "	F.	"	Slight spastic paresis of left arm, much more of left leg	No apraxia right, severe motor apraxia left	Vascular	(Clinical case.)

Now, the interest of the case consists in the association of disease of the central nervous system and myotonia, and the author is at pains to argue that the latter is of central origin and due to impairment of function of the fronto-pontine-cerebellar system. To this matter discussion is directed in a subsequent section.

The cases of tonic innervation here collected are evidently closely related; in each the phenomenon was strictly unilateral, and it was accompanied by other signs pointing unequivocally to the existence of a central lesion. Leaving out those which are not quite sufficiently definite for our purpose, or sufficiently detailed, we have a record of nine—Liepmann 1, Steinert 1, van Vleuten 1, Kleist 1, Goldstein 1, Rhein 1, and Wilson and Walshe 3—on which to base a study of the symptom. And further, of these 5 came to autopsy, while 2 were successfully operated on; hence we have no fewer than 7 to aid us in a consideration of the localization of the phenomenon.

These nine cases belong admittedly to one type, clinically speaking; the occurrence of tonic innervation, or something very like it, in certain other diseases of the central nervous system, will occupy attention in a subsequent paragraph.

TERMINOLOGY AND RELATION TO PERSEVERATION, PROPERLY SO-CALLED.

The term "perseveration" ("perseveratorische Reaktion") was apparently first used by Neisser [30] to express that condition in which the patient repeats a particular act when requested to perform another act, or when he spontaneously wishes to perform another act. To quote from Wilson's [42] paper on apraxia: "The persistence of certain impressions may become a fertile source of error in the execution of complex movements; a patient may recognize an object and use it correctly, but be unable to prevent himself from repeating this act when a different object is presented to him. He may use a spoon properly, but repeat the action of feeding himself with the next thing he is shown, which may, for instance, be a corkscrew." Whether the persisting idea arises spontaneously or secondarily to sense impressions is indifferent. Numerous instances of perseveration are given in the paper from which this excerpt is taken, and to it the reader is referred.

To this variety of perseveration Liepmann [27] has given the name of "intentional perseveration," because it is characterized by the reproduction of a given movement-complex or act when, and only when,

another is intended. The repetition is not independent or spontaneous, so to speak; it occurs only when some new act is intended, and in place of that act, otherwise it would not be noted. It is the commonest form of perseveration, and is well known to the student of nervous and mental disease. According to Liepmann it is found associated mostly with lesions in the posterior third of the brain, especially in the temporal and parietal regions. In our experience it is most often an accompaniment to a degree of agnosia of the auditory or visual variety, but we have also observed it in certain diffuse or generalized intracranial conditions, and we are of the opinion that in the present state of our knowledge it cannot be even tentatively localized.

The term "intentional perseveration," in English at least, is not a satisfactory expression, as naturally it might be taken to signify that the perseveration is intentional, whereas the exact contrary is the case. It is more in accordance with the facts, and at the same time non-committal, to describe this variety simply as "perseveration" without an attached epithet, and this we propose to do.

A second form of perseveration is that in which the patient continues making a particular movement or movement-complex though told to stop: Liepmann's patient, for instance, continued writing hooks and letters though requested to cease writing. The patient cannot put the volitional brake, as it were, on a movement-complex once initiated, but continues to repeat it without apparently making any effort to check it. It is not, however, necessary that the element of continuance against request should enter into the phenomenon. Campbell's patient "continued to shake hands for an unusual length of time." A patient observed by Wilson, writing her name "Winnie" wrote "Winnin-ninninn . . ." indefinitely. A patient of Breukink's [5], peeling potatoes, went on peeling indefinitely, apparently unable to cease. This "Iterativerscheinung" has frequently been noted in cerebral and mental disease.

These varieties of perseveration may occur, as the reader will have seen, in other spheres than that merely of limb-movement. In writing and in speaking, they may also be observed. As the field of speech, however, with its "verbigeration," its "recurring utterances," and its "word intoxication," is somewhat more complicated, it may be left to one side for the present.

Liepmann has proposed to denote the second variety "clonic preservation," because there is alternation or cessation of innervation and then again reproduction of the same. The "tendency to innerva-

tion" persists; the alternation of contraction and relaxation constitutes the "clonic" element in the phenomenon. He opposes it to "tonic perseveration," which, as we have stated, we much prefer to designate "tonic innervation."

We are of the opinion that the expression "clonic perseveration" is as likely to lead to misunderstanding as "intentional perseveration," though for a different reason. It is clear that so-called "clonic perseveration" is a phenomenon of a different nature, on a different plane, from "tonic perseveration," or better, tonic innervation. "Clonic perseveration" is very closely allied to perseveration *sensu strictiori*, in fact, scarcely to be distinguished from it, in certain cases at least. In any case, the terms "clonic" and "clonus" should be reserved for phenomena occurring in the lower levels of the nervous system, and they are erroneously applied to phenomena which are essentially of a psychical or psychomotor nature.

A consideration of the nature of perseveration justifies our assertion that these two varieties are much more closely related to each other than either is to tonic innervation. They are both phenomena which are dependent on a disturbance on the psychical level. They result from the persistence of an idea: Liepmann says it is the "tendency to perseveration" that persists. There is fixation of idea, and as a result the patient executes in succession a series of more or less identical movements whatever be the stimulus on the afferent side. The defect is in the intra-psychical limb of Wernicke's reflex arc. Whether the patient keeps on shaking hands, or shakes hands each time he is asked to perform some other act, the impairment of function derives from a disturbance of psychical order.

Opinions differ as to the explanation of this psychical defect. It is well recognized that an idea possesses a certain duration beyond the time of its clear presentation to consciousness, and Liepmann suggests that the idea of a given movement-complex appears to persist abnormally, and is translated into action again and again, because there are hindrances to the carrying out of other innervations along other paths. As one of his patients made the same perseveration movement first on one side and then on the other, it is clear that not the limb-kinetic element in the movement, but the idea of the movement itself, was at fault, otherwise the phenomenon would have been unilateral. In another place Liepmann postulates an "Unwegsamkeit vieler Bahnen" to explain the persistence of a particular act. Von Sölder [38] is of the opinion that perseveration has its origin in the *active* preponderance

of the persevering idea. In a not dissimilar way Douse, quoted by Pick [33], explains what he calls "opisthomimesis," a condition identical with perseveration. "The mind lags behind the hand and perturbs its action by surviving impressions of what has been already written." Pick [32], on the contrary, holds the view that there is *passive* preponderance of the persevering idea. As a consequence of the diminution of intensity of other ideas, from fatigue, the persevering idea is relatively reinforced and may remain some time. It should perhaps be mentioned that in explaining this diminution of intensity of other ideas as arising from fatigue Pick is arguing from the circumstances surrounding the appearance of perseveration in post-epileptic confusional states, in which he has often found perseveration to occur. Elsewhere, however, he emphasizes the importance of attention in this connexion, and adduces evidence showing that defect of attention may be a factor in perseveration. The patient may be, as it were, in a state of distraction; associations that ought normally to be aroused by the presentation of subsequent ideas are pathologically feeble, and perseveration results. Stoddart [40] speaks of "ideational inertia" as tantamount to perseveration, and his use of the phrase shows that he regards it as equivalent to ideational persistence or persistence of an idea. Some confusion, perhaps, may arise in connexion with the word "inertia." It is a little difficult to understand why inertia of an idea should occasion the actual repetition of the movement-complex which depends on it. An apposite citation from James [18] is given by Pick: "the fact that a certain intensity of the consciousness is required for its impulsiveness to be effective in a complete degree. There is an inertia in motor processes as in all other things. In certain individuals and at certain times (disease, fatigue) the inertia is unusually great, and we may then have ideas of action which produce *no visible act*" (*italics ours*).

This leads us to a last point in the matter of perseveration. In the cases of Kroll, Coriat, and Pick, quoted above, reference has been made to an interesting symptom characterized by apparent cessation of action; during or at the close of the performance of a given act the patient comes to a standstill—either a limb or limbs, or the whole person, as the case may be—in a particular attitude, which is maintained almost indefinitely. The incidents quoted above as illustrative of this condition need not again be particularized. Pick [33], who has devoted much attention to this phenomenon, regards it as a perseverational reaction, and considers that several factors combine to produce it, or rather, that in different cases different factors are at work. He is not certain

whether to consider this "Untätigkeit" the outcome of will-lessness ("Willenlosigkeit") or not, yet he inclines to emphasize the analogy between the state in question and the absence of spontaneity or initiative seen in other cases, in which there is doubtless a true volitional defect.

It would lead us rather away from the main object of this paper to discuss the question of absence of initiative or spontaneity, with its resultant akinesis, in relation to perseveration. Akinesis has frequently been noted in intracranial disease (Hartmann [16], Wilson [42], and others) more especially in connexion with lesions of the frontal lobes and corpus callosum. Etymologically speaking, where action is in abeyance altogether, or where it comes to a standstill prematurely, we are no doubt dealing with a condition of apraxia, and so akinesis may be regarded as true apraxia. But as it is so often associated with a state of generalized mental hebetude and deterioration, no good purpose can be served by an endeavour to link it to apraxia in all cases. Complicating factors, such as inattention and incapacity for retaining impressions, intervene to render its analysis a matter of peculiar difficulty. We are of the opinion, further, that this holds good for that condition mentioned above, which is not, we think, entirely identical with akinesis; the instances referred to above exemplify a condition in which there is normal initiative to begin with, but it speedily exhausts itself; further, sometimes the required movement has been actually completed before the condition of akinesis supervenes.

It is sufficient, then, for our purpose merely to allude to these matters and to point out that whether the cessation of action in these cases, and the passive maintenance of an attitude, is a form of apraxia or akinesis, or not, the phenomenon is at any rate essentially one of a psychical order. Objections might be raised to the view of Pick that it depends on momentary "will-lessness." Though movement come to a standstill visibly, none the less continuance of innervation may be producing this. Liepmann questions whether an awkward attitude would be so preserved in the absence of impulses from the cortex. It may, however, be automatically preserved, no volitional element entering into it, just as a movement may be automatically performed, which the patient is unable to execute on request.

Allusion has already been made to Pick's description of this "akinesis" as a perseverational reaction, which adds yet another connotation to the term perseveration. We are much inclined to

suggest that varieties (1) and (2), viz., the repetition of a given movement in place of another, and the continued repetition of a given movement when in a normal individual it would cease, should be known as *active perseveration*, whereas variety (3)—viz., the cessation of action which results in the maintenance of an attitude either in the middle or at the end of a given movement-complex—should be known as *passive perseveration*.

The description which has been furnished of these phenomena will, we think, have made it obvious to the reader that they are essentially of a psychical nature, and the fact that they are the outcome of a psychical defect distinguishes them *in toto* from tonic innervation—Liepmann's tonic perseveration—where the innervation continues though the patient voluntarily makes every endeavour to inhibit it.

NATURE OF THE PHENOMENON AND RELATION TO APRAXIA.

In our first and second cases the phenomenon of tonic innervation occurred in a pure form. They were uncomplicated by any disturbance of a psychical order, volition in the psychical sense was intact, and no impairment of attention or memory or capacity for retaining impressions was noted. With the best will in the world and with full insight the patients were still incapable of immediately relaxing or inhibiting the contraction of a given muscle or group of muscles on the affected side, although the antagonists were being strongly innervated. The symptom, however, was not always present in unvarying intensity; some attempts at movement in the affected groups were better than others, while occasionally the patients were seen to move the limbs with comparative ease, but this never occurred during examination. In our third case the symptom was observable in equal degree, and, though complicated by other symptoms, its value as compared with the first two is enhanced in that it demonstrated in unmistakeable fashion that the phenomenon was confined to volitional as opposed to automatic or involuntary movements. The patient was incapable of opening her voluntarily closed fist, but on the request "Look at your hand," delivered smartly and unexpectedly, she would automatically open the hand and look at it. She would hold on to the bedclothes interminably, until in response to some stimulus relaxation unexpectedly occurred and the hand was brought up to her face to rub the point of her nose. Similarly, in the first two of our cases, when the limb was left to itself a tonic innervation soon, sometimes immediately, relaxed altogether, in a quite involuntary way.

In a word, the volitional element is the disturbing element; it has been frequently remarked, both in our own cases and in others, that as the patient tried to relax so his grasp perceptibly tightened: and we think the conclusion is justifiable that the variations in duration and intensity are largely due to variation in volition and in voluntary attention.

In saying this, however, we wish it to be clearly understood that we do not mean to imply that imperfection of volition is the *cause* of the phenomenon; if a patient knows what he wishes to do, and voluntarily (and correctly) innervates the antagonists in an attempt to overcome the tonic innervation, his volition is unimpaired; we mean simply that the condition varies with volition, but is not directly dependent on it. In the same way an individual may know a piece of music "by heart" and play it through automatically without being able to begin voluntarily in the middle of it. It is well known that the direction of voluntary attention to an act, in the case of a patient with motor apraxia, may result in that act becoming the more confused. In one of Bonhoeffer's [2] cases the more the patient tried to imitate movements made in front of him the worse was the result. Liepmann's patient was able to execute acts "spontaneously" which he quite failed to accomplish on request. Pick quotes the following passage from a paper by Bernard (which we have not been able to obtain); it is in the words of the patient himself: "I understood perfectly what was said to me and my intelligence appeared to me intact. Yet, having in my hand a common household article, the idea of how to use it completely escaped me, but I had sufficient presence of mind to remember that the best way to get the idea back would be to use the article mechanically without paying the least attention to it: the result was quite successful."

The symptom of tonic innervation, then, is aggravated by voluntary attention, just as other symptoms may be, but volition itself is intact.

The fundamental defect in tonic innervation is not of a psychic, but of a psychomotor nature; the patient is unable to inhibit an innervation which he has correctly initiated. As the affected groups remain in a state of active contraction, there must be continuance of stimulation or innervation at the source of movement, but that this cannot represent a permanent defect in the middle level centres—the motor centres—is plain when we remember that with automatic movements the phenomenon is not observed. We are dealing, therefore, with a psychomotor as opposed to a motor condition, one which corresponds, physiologically

speaking, to an impairment of function at the distal end of the psychomotor (efferent) limb of Wernicke's reflex arc.

We have seen that tonic innervation may occur independently of either dyspraxia or apraxia. Our first two cases prove this definitely. Any awkwardness of movement of the left limbs in these cases could be accounted for by the great difficulty experienced by the patients in passing from one movement to another; the attempts they made to execute given movements were always very fairly recognizable. Similarly, van Vleuten's patient presented the symptom in his right limbs, which were eupractic, while his left limbs were apraxic, but there tonic innervation was wanting. Again, Liepmann's patient had tonic innervation in the limb which was but slightly dyspractic, while the right arm was grossly apraxic, without, however, showing tonic innervation.

The symptom, therefore, sometimes is independent of any concomitant apraxia, and it sometimes occurs in cases where apraxia is conspicuous by its absence. On the other hand, in our Case 3, as in Goldstein's case, and in several of the other cases, the patient was undoubtedly apraxic in the same limb or limbs as presented the symptom or condition of tonic innervation. In view of these facts the latter must be considered an independent symptom and should apraxia occur with it the two should be dissociated for clinical purposes.

RELATION TO THE PYRAMIDAL SYSTEM.

In no one of our three cases was the cortico-spinal system functionally intact on the side which was characterized by the occurrence of tonic innervation on volitional movement. That is to say, an extensor response and ankle-clonus were present, and in the case of the affected arm the tendon reflexes were increased. At the same time, in all three the leg was definitely more involved in the pyramidal defect than the arm, in which little real weakness was to be detected. It is important to bear in mind, also, that as the pyramidal lesion progressed the phenomenon in question diminished, and, in our first two cases, it disappeared after the operation, when a typical hemiplegia developed. From a consideration of our own cases, therefore, the deduction may be drawn that tonic innervation only occurs when the specific functions of the cortico-spinal system are slightly impaired.

This view is borne out by a survey of the other cases in the series. As hemiplegia developed on the right side in van Vleuten's case, so did

the tonic innervation disappear; it was absent when the right hemiplegia was typically present. In this case, it is true, the description given suggests that the specific functions of the pyramidal system may have been normal when the symptom of tonic innervation was first noted. In Rhein's case there was a hemiplegic attitude and some rigidity on the affected side; but the extensor response came later. In Kleist's case the phenomenon was present on both sides, though unequal; the history was one of hemiparesis first on one side and then on the other, and on examination there was slight bilateral spasticity, with brisk jerks and double ankle-clonus. Goldstein's case was one where a left hemiplegia had largely cleared up in the arm and face, while the leg remained badly paralysed. Tonic innervation was present in the arm. Steinert's patient had a right hemiparesis, the leg being more affected than the arm; a right extensor response was present. Liepmann's patient had slight weakness of the face and (?) of the arm at the time when tonic innervation was noted to occur.

The collected evidence, therefore, indicates that the cortico-spinal system for the limb in which tonic innervation is found is not functionally normal; at the same time the involvement must not be too great. Whether the symptom may occur with an intact cortico-spinal system is a little doubtful.

As a corollary, the remark may be made that tonic innervation is not dependent on, nor does it proceed *pari passu* with, hypertonicity of pyramidal origin. The tonus of the affected musculature was only slightly augmented in our cases as in the others that have been recorded. In our Case 3, perhaps, it was rather more marked, as in Kleist's case; yet no definite relation between it and the symptom can be detected. With rigidity and contracture of the right limbs, in van Vleuten's case, there was no tonic innervation on volitional movement.

Evidently no association between hypertonicity and tonic innervation can be established. In progressive lenticular degeneration, as observed by Wilson [43], the musculature is in a state of considerable hypertonicity, but tonic innervation is not found. Whether the latter ever occurs with normal tonus, or with hypotonus, is, again, a little doubtful.

RELATION TO MYOTONIA, PROPERLY SO-CALLED.

One of the most interesting questions in connexion with the phenomenon of tonic innervation is that of its relation to myotonus or myotonia. It was remarked in the introduction to this paper that as

far as the symptom itself is concerned there is little clinical differentiation to be made between it and the myotonus of Thomsen's disease or of myotonia atrophica. The analogies and differences between these we shall now proceed to examine. It should be clearly understood that we are here concerned with a consideration of the symptom only; the complete clinical picture of myotonia congenita or of myotonia atrophica is very different from that of tonic innervation as exemplified by our cases, and no difficulty in reaching a diagnosis should occur.

In myotonia congenita, when the patient suddenly attempts an energetic voluntary movement, the muscles concerned, after being correctly innervated, remain in a state of tonic contraction for a variable period, and although the antagonists are duly innervated the patient cannot relax or inhibit the tonic contraction of the affected group or groups. Such factors as emotion, self-consciousness, cold weather, previous long rest, &c., seem to have an aggravating effect on the symptom, but, speaking generally, the influence of these is neither constant nor very great. The degree to which the volitional element enters into the movements concerned is not important, for, while it is true, as has just been remarked, that the phenomenon comes out with greater distinctness when the movements are forceful, yet it may be seen in more automatic and reflex movements, as in walking, eating, &c. As a rule, also, the impeded movement becomes easier and easier with repetition, until eventually it can be performed in a normal fashion.

In myotonia atrophica, also, the exact relation of which to Thomsen's disease is still in dispute, the myotonic phenomena are practically identical. There is often embarrassment in such imperfectly volitional movements as mastication, moving the tongue, blinking the eyes, &c.

While admitting that the muscular atrophy of myotonia atrophica, the muscular hypertrophy of myotonia congenita, the familial features of these diseases, the peculiarities of the electrical reactions, and so on, will enable the observer to differentiate between them and tonic innervation, we maintain, nevertheless, that as far as the actual symptom of inability to relax a contracted muscular group is concerned, no clear or unequivocal distinction can be drawn between its manifestation in the latter of these conditions as opposed to the former. There is no peculiarity in the symptom, once it occurs, in any one of these diseased states in comparison with the others. The important fact of the occurrence of tonic innervation, generally speaking, only with volitional movement, and not at all with automatic or reflex movement, is an indication that the disturbance of function is cortical or transcortical

in origin, but not that the mechanism involved has a different site from what it possesses in myotonia atrophica and myotonia congenita.

What is the lesion in these two diseases? It has been held very widely that in the latter the essential morbid change is hypertrophy of muscle fibres and that the disease is myopathic. The suggestion has been made, it may be noted, that this hypertrophy of muscle fibres as found at biopsy, is the result of mechanical irritation during excision. Oppenheim and Siemerling [31] have shown that in portions of muscle excised from a living patient an apparent hypertrophy is produced by the contraction of the fibres, which can be avoided if the contraction be allowed to relax. Curschmann [8] has also advanced arguments against the myogenic nature of the affection, and affirms his belief in its central or supranuclear origin. New light has been thrown on the subject from another direction. The investigations of Piper [34] with the string galvanometer have shown that impulses at the rate of some 50 a second reach a voluntarily innervated muscle from the central nervous system. This 50-a-second rhythm is not of myogenic origin. Gregor and Schilder [14] have examined by this method an advanced case of myotonia atrophica, and have shown that during the continued tonic contraction in the affected group the same action-currents of some 50 a second are demonstrable as during prolonged voluntary innervation. In other words, the tonic contraction of myotonia is not a muscular phenomenon pure and simple, but is of central origin. Hirschfeld [17] has also found normal action-currents in cases of myotonia. These physiological investigations are of considerable significance, in our opinion, especially as there is clinical evidence pointing in the same direction. Myotonia has been described several times in association with syringomyelia (Handelsman) [15], in fact a special type has been described as myotonia syringomyelica by Schlesinger [36]. It has been seen in transverse myelitis (Frohmann) [11] and in spinal tumour. As yet apparently only one case of myotonia atrophica has been examined pathologically, by Steinert. In addition to muscular changes associated with the extensive atrophy in the case, there was a well-marked degeneration of the posterior columns of the cord, not unlike what may be seen in tabes. Steinert suggests that this degeneration is not accidental, but possibly an integral feature of the disease. From these facts it may be fairly concluded that there is at least as much evidence to point to a central origin of the myotonic phenomenon as to suggest that it is peripheral.

The view that we take is that the mechanism involved in the

production of myotonia is a spinal cord mechanism, and that the impairment of innervation is an impairment of function of the final common path, to use Sherrington's [37] terminology. Myotonia may occur with spinal cord lesions, and in myotonia congenita there is physiological proof that the defect of innervation is central and not muscular. We are also of the opinion that tonic innervation and myotonia are symptomatologically very closely allied, and that disturbance of the spinal cord mechanism concerned may occur by reason of a lesion at the proximal extremity of the upper motor neurone, as well as by lesions at its distal end. Hence the lesion producing tonic innervation may be cortical. We shall amplify these views in the section that deals with the pathogenesis of the symptom.

RELATION TO CERTAIN INVOLUNTARY MOVEMENTS.

Another interesting question concerns the relation of athetosis, in some cases, to the phenomenon of tonic innervation—a relation which also has bearing on the localization of the symptom.

Some cases of athetosis present a condition identical in every particular to tonic innervation. Thus a patient under the care of Wilson at the National Hospital suffers from right hemiplegia with athetosis, dating from an attack of encephalitis at the age of 8 or 9. The hemiplegia is slight in degree. The patient cannot easily make flexion movements of his right fingers and hand; when he tries, as a rule extension of the wrist and fingers is the result. If, however, he closes the right hand passively with his left, he can then maintain the flexion of the right hand and fingers very well, against resistance. As a rule, further, he can readily open the right hand once it is thus closed. But every now and then he is unable to inhibit the innervation of the flexor groups concerned. The more he endeavours to relax the more strongly does he grasp; if the examiner's fingers are in the patient's hand he can easily convince himself of this. In spite of the tendons of the extensors standing out in contraction, the flexors cannot be relaxed; they may continue for many seconds so that, in fact, the patient says, "My hand remains closed *until I forget about it*, then it opens at once."

An analogous case has been recorded by Kaiser [19], a case of right-sided athetosis and myotonia in a youth, aged 19. "After the muscles are relaxed as completely as possible the patient is asked to execute suddenly any simple movement of the right arm or leg; this is promptly performed, as in any normal individual; thereafter, however, he is

unable to relax the muscles once they are contracted." Grasping a pencil in his right hand, he was unable to let it go for as long as thirty seconds, in spite of immediate innervation of the extensors; "Man sieht wohl, wie die Extensoren sich sofort bretthart anspannen, es bleiben aber die Flexoren ebenso stark contrahirt." The same phenomenon of tonic innervation was present in other muscle groups.

A remarkable case has been published by Mills [29] under the title of "Myotonia and Athetoid Spasm," which is difficult to classify; indeed, it is perhaps unique. The patient suffered from athetoid movements of the left limbs, and involuntary tonic contractions of the muscles of that side effectually prevented him from accomplishing any given voluntary movement satisfactorily. If he wished to grasp an object the extensors would spring the hand open and would remain tonically innervated in spite of every endeavour of the patient to relax or inhibit them. It is not quite clear from the description given by the author whether the phenomenon of tonic innervation, as we have been describing it, existed in this case; it occurred apparently with involuntary as opposed to voluntary innervation, but the whole case is so curious that we are not disposed to lay stress on it. Nevertheless, the indications all pointed to the symptoms being of central origin.

An equally curious case, at one time diagnosed as atypical myotonia, has been recorded by Bremer and Carson [4]. The patient, in addition to suffering from left-sided tonic spasm, sometimes of the sinuous nature of athetoid movements, was frequently unable to relax innervation on both sides of the body. When bringing an axe down on to a block of wood he became immobilized for many seconds in the attitude. The lesion was an angioma of the right cerebral motor area.

A distinction must be drawn, in cases of athetosis, between mere involuntary mobile spasm and the phenomenon under discussion. In athetosis the involuntary innervation of a muscle-group will immobilize the limb, or a segment of the limb, in an athetoid attitude, as in the case of a patient seen by Wilson whose fingers, after a stroke, very frequently assumed a fan-shaped attitude of separation, and it was with difficulty that this attitude was voluntarily checked. But involuntary immobilization in an attitude involuntarily assumed is different from the involuntary maintenance of a contraction *voluntarily* initiated, and continued *in spite of voluntary innervation of the antagonists*. Nevertheless, we suspect that in not a few cases of athetosis, especially such as are mild in degree, the observer will find

that tonic innervation is present in a less well marked or less enduring form. Lewandowsky [25] goes so far as to say that the abnormally long maintenance of a given voluntary innervation can be seen in many cases of ordinary hemiplegia, and that the mildest form of this disturbance is seen in Babinski's *adiadochokinesis*, where the patient is unable to make a succession of quick alternating movements, because he is unable to inhibit quickly enough a given innervation once it is made. Lewandowsky does not consider *adiadochokinesis* the expression of cerebellar defect merely, but says it is found also in slight cases of hemiplegia.

We do not know that we agree entirely with Lewandowsky in this, but, at any rate, it cannot be denied that mild degrees of tonic innervation occur, perhaps also in ordinary hemiplegia, and that it is impossible to draw a hard and fast line between what is to be considered worth noticing and what is to be neglected. If in this paper we have dealt with well-marked instances, we cannot furnish any criterion or standard by which to judge when an innervation is sufficiently long to be designated a "tonic" innervation. If it is maintained beyond the command to relax, it is certainly pathological. The cases we have quoted in this section are, we think, free from objection, and they show that tonic innervation, in the strict sense, may occur in association with *athetosis*. It is practically certain that in the first case the lesion is cortical, and in Kaiser's case it may be so. It is certain that *athetosis* may result from lesions that are essentially cortical (Demange [9]). Where *athetosis* and tonic innervation are associated, the assumption may be made that the lesion is likely to be cortical, the more so as Wilson has shown that *athetosis* has for its basis a disturbance of function of the afferent cerebello-thalamo-cortical path, and the only place where that path and the pyramidal path meet is in the cortex.

PATHOGENESIS AND LOCALIZING VALUE.

The valuable experiments of Sherrington [37] on reciprocal innervation make it extremely likely that certain disturbances of motility may be explained satisfactorily by a disturbance in the proper relation between impulse and inhibition. Reciprocal innervation is readily produceable from the cerebral cortex, but the cortex is not essential to the reaction. Sherrington has shown that it is obtainable by direct excitation of the internal capsule itself, and the reaction there obtained is just as striking. "It is evident," to use his own words, "that the action of arrest may take place in centres which are subcortical." In

case the reader may erroneously imagine that such subcortical centres are constituted by the basal ganglia, he may be informed that we are assured by Dr. Graham Brown that the reaction is obtainable with equal ease from the pyramids in the medulla. Exner [10] inferred from similar observations that the inhibitory phenomena had their chief seat in the spinal mechanisms, though elicited from the cortex, and Sherrington states that "my own inference has been that the seat of inhibition in these reactions from the motor cortex lies probably at the place of confluence of conducting channels in a common path, likely enough at their confluence upon the 'final common path,' the motor neurone, that is at the ultimate synapse."

We are therefore in possession of physiological data which go to show that as a given muscle is innervated, so its antagonists are actively relaxed, and that this reciprocal innervation is carried out in the spinal cord though it may be elicited from the cerebral cortex. This does not exclude the extreme likelihood, as Sherrington says, that in other fields of action one cortical element inhibits another cortical element.

It appears to us feasible to explain the phenomenon of tonic innervation by a disturbance of reciprocal innervation in "willed" movements. Emphasis is laid on the "willed" movements, because it may be remembered that in our Case 3 the phenomenon was typically and solely present on voluntary movement, and not on involuntary movement. As the patient voluntarily contracts his flexors, say, active inhibition of the antagonists, viz., the extensors, takes place; when next he would reverse this action, he is able voluntarily to innervate the extensors, but there is no corresponding inhibition of the flexors. This constitutes the symptom with which we have been concerned, and while, as has been said, we regard it as a disturbance of reciprocal innervation and localize its mechanism in the cord, we are unable in the present state of our knowledge to go further.

But it may be elicited from the cortex. Our three cases are all cerebral; moreover, the site of the tumour in our first two cases, and the position of the lesion in our third case, as deduced by the remarkable similarity of the case to that reported by Goldstein, where the lesion was accurately determined *post mortem*, are practically identical. The maximum disturbance affected the superior frontal gyrus on the right side; and there must have been direct pressure on the adjacent precentral gyrus, as well as on the middle frontal gyrus and the white matter underlying these convolutions. We are well aware of the

unsatisfactory nature of attempts at correlating lesions and symptoms when the morbid agent is a neoplasm ; but in our third case the lesion is vascular, in all probability, and, as already said, by analogy from Goldstein's case we can determine the seat of the disease with accuracy and with less complication from neighbouring disturbances of function.

In a word, there is reason to suppose that the tonic innervation of the left limbs in our patients is associated with impairment of function of the cortico-spinal neurones from a lesion at their cortical end ; either the activity of the affected motor centres is directly interfered with, or, more likely, the stimuli reaching them by short transcortical paths from a hypothetical psychomotor centre placed in the area in front of the precentral gyrus are interfered with.

It may be remarked also that in all the pathologically corroborated cases the symptom was present only on the side opposite to the lesion ; in left hemisphere lesions it was on the right side clinically, and *vice versa*. It cannot be regarded, therefore, as depending on, or indicative of, an impairment of function of the corpus callosum.

We have met with cases of cortical lesions in approximately the same region where the symptom was not observed, and we imagine, therefore, that its appearance represents a stage in the process of interference with the functional activity of the neurones concerned. It will be remembered that in our first two cases the symptom vanished with the removal of the tumour and the onset, for the time, of more definite hemiplegia, and in a previous section we have alluded to its dependence on the comparative integrity of the cortico-spinal tracts. In view of the fact that in our third case the path was open for involuntary or automatic impulses when it was closed, so to speak, for "willed" movements, we may suppose that the lesion is more likely to be such as to produce a transcortical than a directly cortical impairment of function. But in our ignorance of what is meant by volitional as opposed to involuntary innervation our view must remain merely a hypothesis.

Allusion must be made, finally, to the hypothesis advanced by Kleist [22] [23] to explain the phenomenon of tonic innervation of central origin. Kleist imagines a "tonic co-ordinating" apparatus constituted by an afferent and efferent reflex arc ; the former is the cerebello-rubro-thalamo-cortical (frontal) system, and the latter a doubled path—(1) fronto-pontine tract, middle cerebellar peduncle, nucleus dentatus and back to the nucleus ruber, and (2) direct fronto-rubral path. He further postulates an "apparatus for automatic and expression and associated movements," formed by optic thalamus, corpus striatum, and

corpus Luysii; he thinks that the thalamo-frontal and fronto-rubral systems also enter into this apparatus. In his view disturbances of tonus and co-ordination are linked with the former apparatus, while choreo-athetotic movements, impairment of movements of expression, and associated movements, are linked to the latter.

Apart from other considerations, the uncertainty of the anatomical facts in reference to Kleist's second system make it impossible for us to subscribe to his views, which are, for that matter, contradicted by what is known of the pathological basis underlying both chorea and athetosis.

In regard to the first system, Kleist's hypothesis does not, we think, correspond to the facts of physiology to which allusion has already been made, and on which *inter alia* we rely in our explanation of the nature of the phenomenon known as tonic innervation. A spinal mechanism is at fault, and it is thrown out of gear by defective impulses from the cortex. As for the possibility of the fronto-pontine cerebellar or fronto-rubral system being concerned with co-ordination or the maintenance of tonus, it does not concern the subject of this paper.

BIBLIOGRAPHY.

- [1] BATTEN and GIBB. "Myotonia Atrophica," *Brain*, 1909, vol. xxxii, p. 187.
- [2] BONHOEFFER. "Casuistische Beiträge zur Aphasielehre," *Arch. f. Psych.*, 1903, Bd. xxxiv, S. 564.
- [3] BRAMWELL and ADDIS. "Myotonia Atrophica," *Edinburgh Med. Journ.*, 1913, July, p. 21.
- [4] BREMER and CARSON. "A Case of Brain Tumour (Angioma Cavernosum) causing Spastic Paralysis and Attacks of Tonic Spasms," *Amer. Journ. Med. Sci.*, 1890, September, vol. c, p. 219.
- [5] BREUKINK. "Ueber Patienten mit Perseveration und asymbolischen und aphasischen Erscheinungen," *Journ. f. Psych. u. Neur.*, 1907, Bd. ix, S. 113.
- [6] CAMPBELL, MACFIE. "Agraphia in a Case of Frontal Tumour," *Review of Neur. and Psych.*, 1911, vol. ix, p. 287.
- [7] CORIAT. "The Psychopathology of Apraxia," *Amer. Journ. of Psych.*, 1911, January, vol. xxii, p. 65.
- [8] CURSCHMANN. "Ueber partielle Myotonie," *Berliner klin. Wochenschr.*, 1905, Bd. xlii, S. 1175.
- [9] DEMANGE. "Contributions à l'étude des tremblements prae- et post-hémiplégiques," *Revue de Médecine*, 1883, May, vol. iii, p. 375.
- [10] EXNER. "Zur Kenntniss von der Wechselwirkung der Erregungen im Centralnervensystem," *Pflüger's Archiv*, 1882, Bd. xxviii, S. 487.
- [11] FROHMANN. "Ueber einen Fall von Myelitis transversa mit Muskelwogen und eigentümlichen Veränderungen der elektrischen Reaktion," *Deutsch. Arch. f. klin. Med.*, 1906, Bd. lxxxvi, S. 339.
- [12] GOLDSTEIN. "Zur Lehre von der motorischen Apraxie," *Journ. f. Psych. u. Neurol.*, 1908, Bd. xi, Hft. 4/5, S. 169.
- [13] *Idem*. "Der makroskopische Hirnbefund in meinem Falle von linksseitiger motorischer Apraxie," *Neurolog. Centralbl.*, 1909, Bd. xxviii, S. 893.

- [14] GREGOR and SCHILDER. "Zur Theorie der Myotonie," *Neurolog. Centralbl.*, 1913, Bd. xxxii, S. 85.
- [15] HANDELSMAN. "Ein Fall von Syringomyelie mit neuro- und myotonischer Reaktion," *Neurolog. Centralbl.*, 1911, Bd. xxx, S. 418.
- [16] HARTMANN. "Beiträge zur Apraxielehre," *Monatssch. f. Psych. u. Neur.*, 1907, Bd. xxi, S. 97.
- [17] HIRSCHFELD. "Myotonia Atrophica," *Zeitschr. f. d. ges. Neurol. u. Psych.*, 1911, Bd. v, Hft. 5, S. 682.
- [18] JAMES. "Principles of Psychology."
- [19] KAISER. "Myotonische Störungen bei Athetose," *Neurolog. Centralbl.*, 1897, Bd. xvi, S. 674.
- [20] KLEIST. "Kortikale (innervatorische) Apraxie," *Jahrb. f. Psych. u. Neur.*, 1907, Bd. xxviii, Hft. 1, S. 46.
- [21] *Idem.* "Ueber nachdauernde Muskelkontraktionen," *Journ. f. Psych. u. Neur.*, 1908, Bd. x, S. 95.
- [22] *Idem.* "Weitere Untersuchungen an Geisteskranken mit psychomotorischen Störungen," Leipzig, 1909.
- [23] *Idem.* "Der Gang und der gegenwärtige Stand der Apraxieforschung," *Ergebnisse der Neur. u. Psych.*, 1911, Bd. i, Hft. 1/2, S. 343.
- [24] KROLL. "Beiträge zum Studium der Apraxie," *Zeitschr. f. d. ges. Neur. u. Psych.*, 1910, Bd. xi, Hft. 2, S. 315.
- [25] LEWANDOWSKY. "Bemerkungen über die hemiplegische Contractur," *Deutsch. Zeitschr. f. Nervenheilk.*, 1905, Bd. xxix, S. 208.
- [26] LIEPMANN. "Der weitere Krankheitsverlauf bei dem einseitig Apraktischen und der Gehirnbefund auf Grund von Serienschnitten," *Monatssch. f. Psych. u. Neur.*, 1905, Bd. xvi, S. 289.
- [27] *Idem.* "Ueber Störungen des Handelns bei Gehirnkranken." Berlin, 1905.
- [28] *Idem.* "Drei Aufsätze aus dem Apraxiegebiet," Berlin, 1908.
- [29] MILLS. "Myotonia and Athetoid Spasm," *International Clinics*, 1891, April, vol. i, p. 247.
- [30] NEISSER. "65 Sitzung des Vereins Ostdeutschen Irrenärzte zu Breslau," *Allg. Zeitsch. f. Psych.*, 1895, Bd. li, S. 1016.
- [31] OPPENHEIM and SIEMERLING. "Ueber das Vorkommen von Hypertrophie den Primätfasern in Muskelpartikeln, welche dem lebenden Menschen excidirt wurden," *Centralbl. f. d. med. Wissensch.*, 1889, September 28, Bd. xxvii, S. 705.
- [32] PICK. "Etude clinique sur les troubles de la conscience dans l'état postepileptique," *Annales médico-psychologiques*, 1903, Jan.-Fév., vol. xvii, p. 18.
- [33] *Idem.* "Studien über motorische Apraxie," Leipzig and Wien, 1905.
- [34] PIPER. "Elektrophysiologie menschlicher Muskeln," Berlin, 1912.
- [35] RHEIN. "A Case of Apraxia, with Autopsy," *Journ. of Nerv. and Ment. Dis.*, 1908, October, vol. xxxv, p. 619.
- [36] SCHLESINGER. "Die Syringomyelie," Wien, 1902.
- [37] SHERRINGTON. "The Integrative Action of the Nervous System," London, 1906.
- [38] VON SÜLDER. "Ueber Perseveration, eine formale Störung im Vorstellungsablaufe," *Jahrbücher f. Psych. u. Neur.*, 1899, Bd. xviii, S. 490.
- [39] STEINERT. "Cerebrale Muskelatrophie, nebst einem Beitrag zur Casuistik der Balkentumoren," *Deutsch. Zeitschr. f. Nervenheilk.*, 1903, Bd. xxiv, S. 1.
- [40] STODDART. "Mind and its Disorders," London, 1908.
- [41] VAN VLEUTEN. "Linksseitige motorische Apraxie," *Allg. Zeitsch. f. Psychiat.*, 1907, Bd. lxiv, S. 203.
- [42] WILSON, S. A. K. "A Contribution to the Study of Apraxia," *Brain*, 1908, vol. xxxi, p. 164.
- [43] *Idem.* "Progressive Lenticular Degeneration," *Brain*, 1912, vol. xxxiv, p. 295.

DYSSYNERGIA CEREBELLARIS PROGRESSIVA—A CHRONIC PROGRESSIVE FORM OF CEREBELLAR TREMOR.¹

BY J. RAMSAY HUNT, M.D.
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INTRODUCTION.

As *dyssynergia cerebellaris progressiva*, I would direct attention to a chronic progressive tremor disturbance, which seems deserving of differentiation as a definite clinical type of nervous disease.

This affection is characterized by generalized intention tremors, which begin as a local manifestation and then gradually involve in varying degree the entire voluntary muscular system. The tremor which is extreme when the muscles are in action, ceases entirely during relaxation and rest. If this disorder of motility is subjected to more detailed study, it will be found that, associated with the tremor, there is a well-marked disturbance of muscle-tone and of the ability to measure correctly direct and associated muscular movements; the clinical manifestations of this are *dyssynergia*, *dysmetria*, *hypotonia*, *adiadokokinesis* and *asthenia*. All of these symptoms, including the volitional tremor, which is only the extreme expression of the underlying disturbance of muscle-tone and synergy, indicate a disorder of cerebellar function.

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I, therefore, regard this affection with its progressive tendency, chronic course and well-defined cerebellar symptomatology, as an organic disease caused by degeneration of certain special structures of the cerebellar mechanism, which are concerned in the regulation of the tonus and synergies of muscles.

These cases are further distinguished by the absence of true nystagmus, objective vertigo ("Drehschwindel"), cerebellar fits, vestibular seizures and disturbances of equilibrium, symptoms which are so frequently associated with gross lesions of the cerebellum.

The clinical picture is, therefore, strictly limited to a progressive disturbance of synergic control, the most striking characteristic of which is the ataxic intention tremor, which accompanies any movement of the affected part, whether volitional, reflex or automatic.

CHAPTER I.—REPORT OF CASES.¹

CASE 1.—*A woman, aged 47. Onset at the age of 40, with volitional tremor of the left arm. One year later similar involvement of the right arm, followed by gradual extension to the muscles of the head, trunk and lower extremities. The clinical picture is one of generalized, coarse, ataxic tremor on attempting any movement, however slight, which ceases during rest. A study of the motility shows also a disturbance of the cerebellar function, viz., dysmetria, dyssynergia, hypotonia, adiadokokinesia and intermittent asthenia; otherwise the neurological examination is negative. The chief symptom is generalized dyssynergia with tremor movements on intention.*

History.—The patient is a woman, aged 47, born in Germany, of Jewish parentage, who was admitted to the Montefiore Home, in August, 1908, since which time she has been under continuous observation.

Family history.—Her father died at the age of 84; her mother is 83, and still living. The parents were not related. One of her brothers died of "scrofula" at the age of 17, and another brother and a sister died in infancy of unknown causes. No members of her immediate family have been subject to tremors of any kind, nor is there any history of such tendency in the collateral branches.

Previous history.—The menses appeared at 13½ years, were regular and of normal character. Menopause at the age of 40. She married at 24, and was never pregnant. For fifteen years she has been a widow. Previous to her marriage she had been a cook, and this occupation she resumed after her husband's death.

Her only previous illnesses have been an attack of enteritis in the summer

¹ From the Neurological Wards of the Montefiore Home and Hospital.

of 1899, influenza in 1890, and pleurisy in 1892. Otherwise she has been well and strong and in excellent health. She was always moderate in the use of alcohol, as well as tea and coffee. There is no history of mental or physical trauma or of venereal disease. For eighteen years she has had a small, firm enlargement of the isthmus and right lobe of the thyroid gland (without symptoms of Graves' disease).

Present illness.—Onset of the disease seven years ago, with an awkward tremor movement of the left hand on attempting to grasp an object. The intensity of this gradually increased, so that with every effort to move the arm there was an awkward shaking tremor. When the arm was at rest there was no tremor. For an entire year this symptom remained limited to the left arm. At the expiration of this time, the same disturbance of motility (volitional tremor) developed in the right arm, and this in turn gradually increased in severity. In the course of the next year a similar shaking and tremor made its appearance in the head and then gradually extended to the trunk and lower extremities. The speech also became affected.

This peculiar motor agitation has shown slow and steady progress, involving in turn the upper and lower extremities, the head and trunk and the muscles of articulation.

The left arm was first affected, a year later the right arm, a few months after this the head and neck and muscles of articulation; after this there was a steady progressive involvement of the trunk and lower extremities, together with an increase in the general severity of the entire tremor disturbance.

During this period of progression, and occasionally since, she has suffered from headaches in the frontal region, but these were never very severe and have not been frequent. They were not accompanied by nausea or vomiting. There has been no diplopia and no attacks of objective vertigo ("Drehschwindel"). A subjective sensation of dizziness and vertigo is not uncommon, especially when the head tremor is excessive. There were never attacks of spontaneous vertigo in the recumbent posture. She has never had any fainting or convulsive seizures.

There is no subjective disturbance of vision, other than that which would naturally accompany the constant nodding and shaking of the head. There have been no paræsthesiæ, girdle sensations, and no vesical disturbances. There is no tendency to undue hilarity or exaltation, no explosive emotional attacks and no especial depression. Memory is good and the mentality shows no deterioration or change which is worthy of special mention.

She complains of fatigue and dull aching pains in the muscles of the extremities after exertion; but has never been subject to sharp or lancinating pain.

As a rule she sleeps well, and during sleep all trace of the tremor disappears. When any movements in the bed are made, such as a sudden start or turning, the tremor appears and wakes her; when there is any noise or disturbance in the ward she often wakes in tremor.

The tremor.—If the patient is lying in the recumbent posture with the

body completely relaxed and the head supported by a soft pillow, there is no vestige of any movement.

The slightest attempt at innervation, such as fixation of the eyes, a movement of the hand, a simple flexion of the extremities, or even attempts to speak or smile, are sufficient to produce tremor which is usually increased by the patient's attempt at repression. Mental excitement and effort are also effective in aggravating the tremor. The automatic act of respiration alone, when the patient is quiet and relaxed, does not produce a tremor; during the more violent exacerbations of tremor the respiratory movements are sometimes jerky and arrhythmical.

The favourite position of the patient while sitting is leaning forward, resting the head, arms and upper portion of the body on a table. In this position she will often remain for long periods perfectly quiet and relaxed, unless she is questioned or her attention attracted, when immediately more or less violent tremors result.

While sitting quietly in a chair before the examiner with the arms resting on the lap, the tremor may be confined to nodding and shaking of the head, some facial movements and oscillations of the body; but mental excitement or a slight attempt at voluntary innervation, such as speech or movements of the fingers, seem to disturb the balance and adjustment of the patient, and violent tremors result.

There is no true nystagmus. If, however, the tremor is checked by holding the head, tremor will occasionally appear in the eyes. Such oscillations, however, are not obtained by fixation of an object with the eyes. The overflow of tremor also takes place if the movements of an upper or lower extremity are forcibly checked.

The tremor of the extremities is of the volitional or intention type, and consists of a coarse ataxic shaking and tossing of the extremities rather than a true rhythmical tremor, although in certain positions this ataxic shaking assumes a more or less rhythmical character. It reaches its highest degree of intensity in the upper extremities which are sometimes hurled and thrown about with such violence while under innervation, that severe bruises and contusions may result.

On attempting to place the index finger upon the tip of the nose, the arm is jerked and thrown about with ataxic violence, the motor agitation subsiding, and becoming less severe when the object of the movement is finally reached. On attempting to place the heel upon the knee in the recumbent posture, the same coarse volition disturbances appear; and if the leg is elevated, as with the arm, a violent ataxic tremor develops. Closure of the eyes has no appreciable influence upon the extent or character of the movements.

On standing, the general tremor is much increased, the legs shake, the trunk oscillates, the head is in constant movement, and the arms are tossed and thrown about in most bizarre fashion. Because of the severity of the motor disorder the patient receives all her food and drink from the hands of a nurse. This has been necessary for the past three years. Chewing and

swallowing aggravate the tremor, which adds still more to the difficulty and embarrassment in taking nourishment.

Static equilibrium is well maintained even on a narrow base, and closure of the eyes in this position has no apparent effect upon posture or the intensity and character of the tremor.

For some years all finer movements of the hands have been impossible, and for several years the handwriting has been reduced to illegible scrawls and scratches.

If the patient has had an exciting or fatiguing day, some after-tremor may persist for several hours, even during the period of rest.

On several occasions, during the years of observation in the hospital paroxysms and crises of tremor have occurred, lasting for weeks at a time, in which all of the tremor symptoms have been greatly exaggerated. During this crisis of tremor, standing and walking were difficult and precarious, because of the violence of the motor agitation. After a time, however, the crisis diminishes, equilibrium is restored, and there is a return to the original degree of disability which is chronic and permanent.

The tremor is usually more severe in cool weather.

The speech is slow and scanning and is frequently broken and interrupted by violent explosive efforts and utterances. Under excitement these brusque explosive discharges render it almost unintelligible. The speech disturbance is evidently caused by the same disharmony which characterizes the other muscular efforts. During the act of articulation there are associated tremor-like contractions of the facial movements, and the tremor of the head is much exaggerated.

Asthenia.—There is no paralysis of the muscular system in the usual sense of the word, and the initial muscular effort is carried out with approximately the normal degree of force. There is, however, a curious asthenic symptom of an intermittent character. This is characterized by the inability to sustain or fix a muscular contraction except for short periods of time. If, for instance, the patient is instructed to grasp the hand of the examiner and to maintain the grasp, it is found that the initial effort is of normal force, but after 5 to 10 seconds the grasp relaxes in spite of every effort to maintain the contraction. Immediately after the relaxation of the hand, which is involuntary, another effort is again made, only to suffer the same spontaneous relaxation; so that instead of a single sustained contraction, we are confronted with a series of brief, intermittent muscular contractions of fair intensity. This inability to sustain a muscular contraction, I would designate *intermittent asthenia*, as the clinical impression produced is that of asthenia, although it is not improbable that the underlying disturbance is very closely related to the dyssynergia which will be referred to later.

The intermittent asthenia may also be demonstrated in other muscles of the extremities, as in flexion and extension of the wrist and elbow, abduction of the arms and in the various movements of the legs. It is therefore, like the tremor, a generalized manifestation.

On a few occasions, the patient has suddenly fallen to the ground, because of the giving way of one of the legs when attempting to stand in one position, as before a looking-glass in preparation of her toilet. Such falls are apparently due to an intermittent asthenia of the lower extremities, and are unaccompanied by vertigo or obscuration of consciousness. The electrical reactions of the muscles are normal, both quantitatively and qualitatively. It is interesting to note that strong faradic currents produce sustained muscular contractions without the intermittent relaxation which accompanies voluntary movements.

Hypotonia.—The muscles are well developed and free from atrophy. They are, however, soft and flabby to the feel and there is present a definite hypotonia. The joints are relaxed and flaccid and may be over-extended. This is present in both the upper and lower extremities, and especially in the arms. If the arms are watched during the volitional tremors, it will be seen that, especially in the movements of the hands and fingers, extreme attitudes indicating hypotonia are assumed.

The Stewart-Holmes sign of hypotonia is also present in the upper extremities, i.e., the failure of rebound or recoil when flexion of the arm is resisted and suddenly relaxed. The flexion movement continues until mechanically checked without the intercurrent contraction of the antagonistic triceps. The mechanical irritability of the muscles on percussion is normal; no myotonic phenomena are present.

Dysmetria and dyssynergia.—When the individual movements of the extremities are carefully analysed, a distinct disturbance of the ability to measure, regulate and harmonize voluntary movements is found. In order to eliminate the tremor as far as possible, so that isolated muscular movements may be studied, it is best that the patient be placed in the recumbent posture with the arms relaxed and the head supported. In this position complete motor relaxation and quiet may be produced. If the patient is instructed, with the arm resting on the bed or upon a table, to elevate the index finger and then allow it to fall and to continue repeating this single movement, a number of interesting phenomena become apparent. These tests may also be made with the patient sitting in a chair with the arm relaxed and resting on a table.

This test movement of the index finger is produced by the contraction of the extensor indicis, which is immediately relaxed. Instead of the normal elevation and fall of the finger as should occur, an overaction is observed. The index finger is thrown brusquely as high as possible and remains fixed, relaxation not taking place immediately. Or instead of a single extension movement there may be two or sometimes three successive attempts before the finger is brought into extension. It will also be observed that instead of allowing the finger to fall by simple cessation of contraction, there is an overaction of the antagonists and the finger is thrown down, striking the table with some force.

If the forearm of the patient is encircled by the examiner's hand during these efforts, it will be found that there is a synchronous contraction of the

flexors (antagonists) of the forearm and also occasionally in the muscles of the upper arm.

These symptoms of dysmetria and dyssynergia, which may be demonstrated with ease in the contractions of single muscles, are also very evident in the larger and more complicated movements of both the upper and lower extremities, but may be overlooked and masked by the general tremor which is produced.

Adiadokokinesis was distinctly present in both upper extremities. On attempting to perform quick alternating movements of supination and pronation the movements are slow and interrupted, and there is an inability properly to control and measure them, so that a quick rhythm of normal rapidity is impossible.

This disturbance may also be demonstrated in the movements of the index finger and thumb, preferably tested while the arm is relaxed and resting upon a table.

Sensation.—The general sensations, both superficial (touch, pain and temperature) and deep (muscular and articular), are entirely normal. There is no demonstrable defect in the ability to distinguish the relative difference of weights placed in the hands.

Vision, the sense of smell, taste and hearing are normal and equal on the two sides.

The Bárány rotation and caloric tests show the normal nystagmus reactions on both sides. These reactions are delayed and are obtained with some difficulty, requiring strong stimuli for their production. This is probably due to a certain diminished sensitiveness of the peripheral apparatus of equilibrium by reason of the constant violent oscillations of the head.

The pointing tests ("Vorbeizeigen") are difficult of interpretation because of the violence of the volitional tremor.

Reflexes.—The tendon reflexes of the upper extremities (supinator biceps and triceps jerks) are present, not exaggerated, and are equal on the two sides. The jaw-jerk is present and not exaggerated. The knee-jerk and ankle-jerk are present on both sides and are of equal intensity and not exaggerated. The abdominal reflexes are present and equal. The plantar reflex gives a normal flexor response on both sides, and the Babinski reflex has not been demonstrable during the many years of observation in the hospital.

Cranial nerves.—The pupils are equal and react promptly to light and accommodation; the pupillary skin reflexes are normal.

Ophthalmoscopic examination shows normal optic nerves; no signs of neuritis or pallor of the disc. The ocular excursions are normal, no true nystagmus. The innervation of the facial muscles, the muscles of mastication, soft palate and tongue is normal, but produces marked tremor disturbances.

General examination.—The apex beat is in the fifth interspace within the nipple line. There is a systolic murmur over the body of the heart; the second sounds are not accentuated. Percussion of the lungs and the breath sounds are normal. Percussion and palpation of the abdomen are

negative. There is a slight, firm enlargement of the isthmus and right lobe of the thyroid gland without pulsation or bruit, tachycardia, exophthalmus or other symptoms of Graves' disease. The urine is normal.

The blood contained 4,720,000 red cells; 62,000 white cells; hæmoglobin, 88 per cent. Wassermann tests of blood and cerebrospinal fluid are negative. There was no increase of cells or globulin in the cerebrospinal fluid. There is a marked dermatographia, but no pigmentation of the skin or cornea. The gynaecological examination showed no abnormality.

CASE 2.—A woman, aged 29; onset at the age of 23, with volitional tremor of the left leg. Two years later the left arm showed similar involvement: one and a half years after this the right arm became affected. Since then increase in severity and gradual extension to the head, trunk and right lower extremity. With the tremor are the associated symptoms of a cerebellar disorder, dyssynergia, dysmetria, adiadosokinesis, hypotonia, and intermittent asthenia: otherwise the neurological examination is negative. The clinical picture is one of generalized intention tremors which cease when the muscles are not in action.

History.—Patient is a married woman, aged 29, of Jewish parentage, who has been under my personal observation for the past year and a half.

Family history.—Her father died of tuberculosis at the age of 45; her mother is still living and is in good health; two sisters and one brother are living and well; two brothers died in early life of unknown causes. There is no history of tremor in the family.

Previous history.—Menses began at the age of 13, are regular but somewhat painful. She married at the age of 24, and has been twice pregnant, bearing healthy children; she has had no miscarriages.

She had measles, diphtheria and scarlet fever before the age of 9 years. With these exceptions she has had no illness and has been in good health until the onset of the present disease. She does not take alcohol and is moderate in the use of tea and coffee. There is no history of luetic infection, physical trauma or mental shock.

Present illness.—The affection from which she now suffers first made its appearance six years ago with tremor of the left leg. On standing or walking the leg is subject to jerky, irregular movements, which interfere with the free and easy motion of the extremity. There is no paralysis, no paræsthesiæ, and no pain; when the leg is at rest or in the recumbent posture all tremors cease. Occasionally, however, after fatigue and excitement some tremor persists in the ankle-joint for a short time.

For two years the disturbance was confined to the left lower extremity, gradually increasing in severity. At the expiration of this time the left arm began to show some involvement. Any attempt to grasp an object was accompanied by irregular awkward movements, which ceased as soon as the arm was placed at rest.

One and a half years later a similar tremor appeared in the right arm and has gradually increased in severity.

During the past year the head and trunk show evidences of tremor, and the speech is slow and slightly dysarthric. There is also some tremor in the right leg, so that at the present time there is a generalized intention tremor which affects both upper and the left lower extremity and in a lesser degree the other voluntary movements.

For the past three years all finer movements of the hands have been impossible. It is very difficult for her to eat and drink, and the handwriting is an illegible scrawl. She has at times been able to do coarse work about the house, such as required no special accuracy of movement.

During the course of this affection she has suffered from occasional headaches, chiefly frontal. These occur especially during the menstrual periods. She has had no obvious attacks of vertigo and no diplopia. Occasionally when the head tremor is most severe a sensation has been present of giddiness and lightness in the head. She has had no epileptiform or fainting attacks. The sleep is fair and is undisturbed by any tremor. There are no sphincter disturbances. Her memory is good and there are no evidences of mental deterioration; no emotional crises, and no attacks of forced laughing or crying.

The symptoms have been strictly limited to a chronic, coarse tremor of the intention type, beginning in the left leg and gradually extending to the other extremities, including the head and trunk. This tremor produces some disturbances of gait and station, a marked limitation of the use of the arms, more or less constant nodding and oscillation of the head when held erect, and a slight difficulty in articulation.

The tremor.—If the patient is at rest in the recumbent position, with the head supported and the arms and legs completely relaxed, so that all voluntary muscular innervation is eliminated, there is no sign of tremor. The muscles of the extremities are in a state of perfect rest and quiet. The only exception to this rule is following periods of mental excitement and physical exertion, when some after-tremor may persist for a time; but this passes away if the rest is prolonged. Any attempt, however slight, to carry out voluntary movements—as, for example, fixation of an object with the eyes, a movement of the hand or leg—causes an immediate disturbance of muscle equilibrium, and coarse tremor movements appear in the corresponding region of the body.

In the erect posture, if the patient stands upon a narrow base, there is no sign of ataxia with the eyes either opened or closed. There is simply a nodding and shaking tremor of the head with some oscillation of the trunk and more or less coarse tremulousness of the arms and legs. In walking there is no ataxia in the ordinary sense, but the gait is jerky, uneven and the rhythm and harmony of movement is disturbed by the coarse tremor.

If an attempt is made to place the index finger upon the tip of the nose, the arms are immediately thrown into the violent motor disorder which characterizes the intention tremor. The same is true of the left leg, and to a less extent of the right leg when the heel is carried upon the knee of the opposite leg.

If the arm or leg is elevated, the extremity is immediately thrown into a violent atactiform shaking tremor, which ceases as soon as the voluntary

innervation is removed and the part is placed at rest. Even slight voluntary movements, as of the fingers or hand, tend to produce considerable motor disorder of the whole extremity, unless the voluntary innervation is checked and the part placed at rest.

The speech is slower than normal and slightly scanning and at times uneven and slightly dysarthric. Mastication and deglutition are performed without difficulty, but are associated with an increase of the head tremor. There is no tremor of the facial muscles.

Asthenia.—The gross motor power of the extremities is undisturbed. There is, however, an intermittent asthenia or inability to sustain, except for brief periods of time, a co-ordinated muscular movement. For example, on attempting to maintain a hand clasp, in spite of every effort the grasp will relax and another attempt must be made, which in turn is only of short duration; so that instead of a single sustained contraction of the muscles concerned in maintaining a grip of the hand, there occurs a succession of interrupted efforts towards the same object. This may also be demonstrated in flexion of the elbow, extension of the foot or any other voluntary movements in which such a test could be carried out.

The electric excitability of the muscles to both faradic and galvanic currents shows no deviations from the normal. With strong faradic currents, tonic contractions of the muscles may be produced without the intermittent relaxation noticed in voluntary effort.

Hypotonia.—The muscles are fairly well developed and show no signs of atrophy. They are, however, soft and flabby on palpation and the joints are relaxed and flaccid. This is especially true of the upper extremities, in which the Stewart-Holmes sign of hypotonia is present. Mechanical irritability of the muscles is normal on percussion.

Dyssynergia and dysmetria.—If the arm is placed in a relaxed position and the muscular contractions of single movements are studied, there will be found evidences of dyssynergia and dysmetria. This is even more apparent in an analysis of the more complicated co-ordinated movements of the extremities, although somewhat masked and less readily identified because of the marked generalized tremor disturbance which results.

Adiadokokinesis is present on both sides.

Sensation.—Superficial and deep sensibility are entirely normal. There is no demonstrable defect in the ability to determine the relative difference of weights placed in the hands.

Vision, smell and hearing are normal. The Bárány rotation and caloric tests produce the normal nystagmus reactions, showing the integrity of the labyrinthine apparatus on both sides. The pointing tests are difficult of interpretation because of the coarse tremor.

Reflexes.—The supinator, triceps and biceps jerks are present, not exaggerated, and are equal on the two sides. The jaw-jerk is present and not exaggerated. The knee-jerks are active, slightly exaggerated and are of equal intensity on the two sides. The Achillis jerks are present and equal on the

two sides. There is no patellar clonus and no ankle clonus. Frequent examinations have shown that the abdominal reflexes are constantly present and equal on the two sides. Plantar stimulation produces normal flexion of the toes. (No Babinski.)

Cranial nerves.—The pupils are equal and react promptly to light and accommodation; the pupillary skin reflexes are present. The ocular excursions are normal; no nystagmus. Ophthalmoscopic examination of the optic nerves is negative. There is no pallor of the disc and no sign of neuritis. Innervation of the face, muscles of mastication, soft palate and tongue are normal.

General examination.—There is a moderate degree of dermatographia; no pigmentation of the skin or cornea. The heart and lungs are normal; urine is normal.

Wassermann tests of the blood and of the cerebrospinal fluid are negative. There is no increase of the cellular elements or of the globulin content of the cerebrospinal fluid. Abdominal palpation and percussion are negative. No enlargement of the thyroid gland.

Gynæcological examination shows multiple stellate lacerations of the cervix, anteversion of the uterus and a mass in the right broad ligament with thickening of the Fallopian tube. The ovaries are normal.

CASE 3.—*Onset of the disease in a man, aged 28, with intention tremor of the right arm, followed six months later by a similar disturbance of the left upper extremity; gradual extension to the head and muscles of articulation. Slight involvement of the lower extremities; otherwise the neurological examination is negative. The clinical picture consists of intention tremor of the upper extremities, with involvement of the head, speech, and in a lesser degree of the legs. In the upper extremities, dyssynergia, dysmetria, adiadosokinesis, hypotonia and intermittent asthenia are associated with the tremor.*

History.—Patient is a man, aged 31, a native of Bohemia who has lived in the United States for the past six years. He is a labourer by occupation, is married, and has two children living and well. His wife has had no miscarriages. There is no history of tremor in the family, and his parents are still living and in good health. There is no history of venereal disease and no trauma. He is unable to give any satisfactory data as to the diseases of early childhood, but since that time he has always enjoyed robust health and has had no serious illnesses.

Present illness.—The disease from which he now suffers made its appearance a little over three years ago, with a shaking tremor of the right hand on attempting any movement. This gradually increased in severity; six months later a similar tremor made its appearance in the left arm and gradually progressed. Following this, oscillations of the head appeared while sitting or standing, together with a disturbance of speech. Later the lower extremities became somewhat affected, but in a less degree.

There have been occasionally frontal headaches since the beginning of the tremor, but they are not severe and are unaccompanied by nausea and vomiting.

He has had no vertiginous seizures, and no diplopia. There have been no pains in the extremities, no paræsthesiæ, no vesical disturbance, no attacks of forced laughter or crying, no fainting and no convulsive seizures. Because of the tremor, the man was forced to abandon his occupation, which consisted of general work of a coarse nature. Movements of the arms, as are required in dressing, eating and drinking, are rendered very difficult and almost impossible by reason of the coarse volitional tremor. There are no subjective disturbances of sight or hearing, and apart from the tremor disturbance his general health is good.

Tremor.—In the recumbent posture, with the head supported there is no visible or palpable tremor movement of the head, trunk or extremities. If, however, the arm is elevated there immediately develops a coarse shaking volitional tremor, which continues as long as the innervation is maintained. If the arm is replaced by the side and voluntary innervation is interrupted, all tremor immediately ceases. The same tremor disturbance is present in the left arm and to a lesser extent in the legs.

If, when lying in the recumbent posture the leg is elevated or an attempt is made to place the heel upon the knee, a coarse shaking and volitional tremor makes its appearance. If the forefinger is carried to the nose, violent tremors of the intention type are produced. It is impossible for the patient to carry a glass of water to the lips without forcibly spilling the contents.

On standing there develop nodding and oscillation of the head. There is also a slight palpable tremor of the lower extremities and some oscillation of the trunk in the erect posture. After excitement or prolonged examination some after-tremor may persist in the recumbent posture, but soon passes off with the rest.

The tremor movement is slow, ranging from three to five per second. The rate and amplitude are increased by excitement and effort. The gait is but little disturbed. The patient can walk a fairly straight line, and the chief manifestations during walking are the shaking of the arms and head. There is no tremor of the face or of the eyes; no nystagmus. The speech is slow and scanning in type, and becomes dysarthric and difficult to understand during excitement.

Asthenia.—The gross motor power of the arms and legs is undisturbed. In the upper extremities, however, there is a distinct inability to sustain prolonged muscular contractions (intermittent asthenia). This is not so evident in the lower extremities where the tremor is comparatively slight.

Hypotonia.—The muscles are well developed and show no signs of atrophy. There is, however, some hypotonia of the upper extremities. The joints and muscles are flaccid and relaxed and the Stewart-Holmes sign of hypotonia is present.

Dyssynergia and dysmetria.—If single movements are studied, like those of the extensor indicis, evidences of dyssynergia and dysmetria are demonstrable. These are also present in the larger movements of the upper extremities and to a lesser degree in the lower extremities.

Adiadokokinesis is present in both upper extremities.

Sensation.—Superficial and deep sensibility are normal. Vision, smell and hearing are normal.

Reflexes.—Supinator, biceps and triceps jerks are equal and normal. The knee-jerks are present and equal, not exaggerated. The ankle-jerks are present and equal, and there is no clonus. The cremasteric and abdominal reflexes are present and equal. Plantar stimulation produces flexion of the toes; no Babinski.

Cranial nerves.—Pupils are equal and react promptly to light and accommodation. Ocular excursions are normal; no nystagmus; the optic discs are normal in appearance. Innervation of the soft palate, tongue, and muscles of mastication are normal.

General examination.—Patient is a strong, robust looking man; no pigmentation of the skin or cornea. Heart and lungs are normal; urine is normal. Wassermann tests of the blood and cerebrospinal fluid are negative. No increase of cells or of globulin in the spinal fluid.

CHAPTER II.—ANALYSIS OF THE SYMPTOMATOLOGY.

General remarks.—The three cases which have been described are similar in their symptoms and clinical course. They differ only in degree and in the duration of the disease.

In all, the symptomatology is limited to a more or less generalized tremor during muscular activity, which is especially severe in the extremities. Associated with and underlying the volitional tremor, are symptoms of dyssynergia, dysmetria, adiadokokinesis, asthenia and hypotonia. In all other respects the neurological examination is negative. There is no nystagmus, no objective vertigo, no disturbances of the static or kinetic equilibrium, and no convulsive seizures. The intellectual functions are intact and the optic nerves are normal. Occasional frontal headaches were observed in all of the cases. These were never severe and were not associated with nausea or vomiting. Subjective sensations of giddiness and vertigo were present at times, especially in Case 1. This was not associated with a feeling of rotation or of movements of external objects, and was apparently caused by the constant shaking of the head. In none of the cases was there a family history of tremor, or evidence of a tremor tendency before the onset of the disease.

The tremor.—The intention tremor is the most striking and characteristic symptom of the disease. This begins in one extremity and progresses slowly, involving gradually and successively the remaining

portions of the body. Three or four years were required for the tremor to become generalized. It consists of a coarse, irregular, atactiform shaking or "Wackeln" on attempting any movement. The tremor movement is slow, ranging from three to five vibrations a second; both the rate and amplitude are increased by mental and physical activity. It ceases entirely in a relaxed or recumbent posture and is consequently absent during sleep. It may happen, if the paroxysms of motor agitation have been prolonged and severe, that some after-tremor may persist, even during rest. This, however, is only observed after unusual efforts or excitement and is of short duration, gradually subsiding with rest and quiet.

If in a relaxed or recumbent posture with the muscular system quiescent, the slightest attempt is made to innervate a muscle, the tremor immediately reappears. It will sometimes happen that the head and extremities are not well supported in the recumbent posture, and some motor perturbation continues even in a state of apparent rest; this persists until the patient is placed in a more favourable position in which the muscular relaxation is complete.

In its severer form, the gait is affected and becomes jerky and uneven, the head is in constant and violent oscillation, the face tremulous, speech scanning and explosive, and the arms are tossed and thrown about in a most bizarre and random manner. In this state of general motor agitation the appearance of Huntington's chorea is more or less suggested, except that the character of the movements is irregularly tremulous rather than choreiform. There is no true nystagmus on fixation of an object with the eyes. If, however, the tremulous shaking head is firmly held and the tremor thus checked, it may overflow and reappear as an oscillation of the ocular movements. At times there are spontaneous rhythmical and rolling movements of the eyes. These may also occur on fixation of an object and are related to the general motor disturbance, and have not the character or constancy of true nystagmus.

There are days, and sometimes longer periods of even weeks, during which the tremor suffers temporary exacerbations. After the subsidence of these crises of tremor there is a return to the usual chronic condition. The whole course of the disease is chronic and slowly progressive, and the motor life becomes more and more restricted; so that the patients in time are almost entirely dependent upon the care of nurses or relatives. Once established, the tremor never disappears, except during rest. In one patient it was exaggerated by cold.

Those muscles which are concerned in the performance of certain automatic functions, like the diaphragm and intercostals, show but slight involvement, and this only during paroxysms of tremor. On such occasions, jerky respiratory movements are not infrequent; at rest in a recumbent position the breathing is regular and uninterrupted. The large muscles of the trunk are but little affected in comparison with the extremities; this is shown by oscillations and tremulous movements of the body in the sitting and erect posture, and by occasional contractions and stiffening of the abdominal musculature.

The tremor is therefore greatest where the voluntary muscular activity has reached its highest degree of functional development and differentiation, as in the upper and lower extremities, and in the head and neck.

The dyssynergia and dysmetria. — The general disturbance of motility is so gross in these cases, that in order properly to study the motor phenomena it is necessary to analyse such movements as require the contraction of a single muscle only or of a small number of muscles. A study of isolated single movements will reveal immediately a difficulty in controlling the measure and association of such movements (dysmetria and dyssynergia). The movement occurs too brusquely or with undue force, so that the aim is over-reached; or it may be insufficient and fall short of the object. This disturbance is usually greater on first efforts or if it be requested that the movement be performed quickly.

Closure of the eyes has no apparent effect upon these motor disturbances, which are very evident in the various segments of both the upper and lower extremities, but which are to a large extent concealed and masked by the tremor.

As a preliminary to performing these tests, the patient should be placed in a recumbent or sitting posture with the arm relaxed and supported by a pillow, preferably with the hand prone. In this position all spontaneous tremor may be eliminated. If the patient is then requested to raise (extend) and then drop the index finger, a disorder of the movement becomes evident at once. In an effort to repeat rapidly the movement of lifting and then letting fall the index finger, it is over-extended and is held fixed in this position of over-extension, and immediate decontraction does not take place; or it may be that two or even three successive attempts are first made before the finger is brought into a position of extension. Then instead of the simple normal relaxation which would allow it to fall almost by its own weight, it is brought down with undue force by a contraction of the flexor muscles. In

other words, there is an inability to carry out quick, rhythmical movements, requiring contractions and relaxations of a very simple kind.

If during these attempts at rhythmical extension of the index finger the muscles of the forearm are encircled by the examiner's hand, it will be observed that with the effort to contract the extensor indicis strong simultaneous contractions of the flexor muscles of the forearm frequently occur, indicating a disturbance in the harmony of the association mechanism of movement (dyssynergia). Such disturbances of the synergy and the measure of movements are even more apparent when larger and more complicated co-ordinated acts are attempted, such as extension of the hand, flexion of the forearm, and the like.

The presence of these disorders of motility gives an insight into the true nature of the tremor, and explains the general motor agitation which is produced whenever the muscular system is thrown into action. With the very evident lack of control in regulating single movements, it does not seem surprising that the patient is utterly at sea in the effort to control the muscles during the activity of an entire extremity. In the effort to control and regulate the muscle synergies under these conditions we have produced the coarse atactiform tremor which is characteristic of the disease.

Adiadokokinesis.—The adiadokokinesis of Babinski is also typically present in these cases. Because of the tendency to general tremors of the arm, this symptom may also be tested to advantage with the arm relaxed and the hand resting on a table. In this position, it is apparent that the power to perform quick successive rhythmical movements is very much diminished. The initial movement is prolonged or insufficient, relaxation does not take place at the proper time, and the succession movements are therefore slow and interrupted. The close relationship of this symptom to the dysmetria and dyssynergia is also very evident.

Intermittent asthenia.—Although the patients tire readily, there is no true paralysis in this group of cases. There is, however, a curious disturbance of the innervation which is best designated as intermittent asthenia. This consists of an inability to sustain or fix muscular contractions except for brief periods of time. For example, if a patient is asked to grasp the hand of the examiner and to maintain the grip firmly, this is found to be impossible. The patient grips the hand firmly at first, and sustains the contraction for a few seconds (five to ten seconds), when spontaneous relaxation takes place. Another attempt is then immediately made only to suffer relaxation again, and even with the greatest effort the contractions cannot be sustained, and are interrupted by spontaneous and involuntary relaxations.

Again, if an attempt is made to hold out the extended arm at right angles, it will be observed that in spite of every effort it tends to fall from the horizontal position and is again thrown back into the horizontal. After this effort has been repeated a few times the arm suddenly falls to the side, the patient apparently being unable any longer to sustain the muscular contractions. After a short period of rest the test may be repeated but with the same result. This inability to sustain contractions may also be demonstrated in flexion movements of the arm, dorsal flexion of the foot, abduction of the arm; in short, any of the movements of the extremities. The efforts to carry out such tests of the motor power are accompanied by considerable fatigue.

In the demonstration of this test, as in those for the dysmetria and dyssynergia, it is preferable that the arm be relaxed and at rest on a table, thus eliminating as far as possible the volitional tremor.

In some respects, this symptom of intermittent asthenia is the reverse of what Babinski has described as cerebellar catalepsy, the ability to fix unduly and immobilize a movement. It is possible that the cerebellar catalepsy is an irritative or spasmodic manifestation while the intermittent asthenia results from the loss of certain cerebellar functions of control.

It is of interest to note, that the intermittent relaxation does not occur when the muscles are contracted independently of the will by strong faradic currents.

Hypotonia.—In the recumbent posture with the muscular system relaxed, palpitation shows the muscles of the extremities to be soft and flabby and the joints unduly relaxed and flexible. This condition of hypotonia is present in both the upper and lower extremities, more especially in the arms. This is by no means so extreme as in certain cases of tabes dorsalis, and while the joints may be unduly extended, the limbs cannot be placed in those abnormal attitudes which is sometimes the case in the severer forms of spinal hypotonia.

The Stewart-Holmes sign of hypotonia in the upper extremities is present: i.e., a failure of the recoil or rebound on resisting a flexion movement of the arm and suddenly releasing it. In performing this test, it is found that the flexion movement of the arm after its sudden release is continued until mechanically checked, there being no reflex contraction of the antagonists, the extensors of the upper arm.

The myotatic irritability of the muscles is unchanged and the tendon reflexes are of normal intensity, showing neither special increase nor diminution.

CHAPTER III.—DIFFERENTIAL DIAGNOSIS.

In general appearance, the motor disturbance which characterizes the progressive cerebellar dyssynergia is similar to the intention tremor of multiple sclerosis. It differs, however, in the slow and gradual manner of progression and the strict limitation of the symptomatology to tremor and the associated dysmetria, dyssynergia, hypotonia, and intermittent asthenia.

All other symptoms of multiple sclerosis, such as nystagmus, objective vertigo, pyramidal and sensory tract symptoms, temporal pallor, hemiplegic attacks, forced laughter, alterations of the reflexes are absent; so that a cerebellar type of this affection may be reasonably excluded.

The pseudo-sclerosis of Westphal may also be eliminated by reason of the strict limitation of the symptomatology to the volitional tremor, together with the absence of mental deterioration, pigmentary deposits and the other symptoms which characterize the recorded cases of this obscure affection.

The theory of a functional disturbance, in the nature of hysteria or the traumatic neurosis, is not tenable in the absence of an adequate etiological factor, and the mental and somatic symptoms which characterize these affections.

The rare tremor type of Parkinson's disease may likewise be excluded by reason of the nature of the tremor and the existing hypotonia and dyssynergia, which differ fundamentally from the muscle manifestations which characterize this affection.

Huntington's chorea, athetosis and myoclonus multiplex are readily differentiated by the character of the motor disorder and persistence during muscular relaxation.

Of especial importance from the diagnostic standpoint is the group of the so-called essential, hereditary or family tremors, the first systematic description of which was given by Dana in 1887. In the original description of this affection the clinical picture was defined by Dana [3] as follows: "The affection in question consists of a fine tremor, constantly present in typical cases during waking hours, voluntarily controlled for a brief time, affecting nearly all the voluntary muscles, chronic, beginning in very early life, not progressive, not shortening life, not accompanied with paralysis or any other disturbances of motor function. It resembles to some extent the tremor of paralysis agitans, still more a simple neurasthenic tremor. It ceases during

sleep, and can be inhibited temporarily by the will. It does not interfere with delicate co-ordination. It neither stops nor increases on ordinary voluntary movements."

At the present time there is an extensive literature treating of this subject (Flatau [4]), the great majority of the recorded cases coinciding in the main with the clinical picture as outlined by Dana. In a few, however, the tremor is described as coarse ataxic and of the intention type, and especially in those cases recorded by Minkowski [6] and Graupner [5] the tremor was gradually progressive and of a severe intention type. The resemblance of such cases to those which are the subject of this study is very striking, and it is not improbable that some of the cases which are now grouped with the hereditary and essential tremors would show on closer examination the same progressive disturbances of the cerebellar function as do the cases which are the subject of this study. It is certainly desirable that the cases of so-called hereditary and essential tremor should be approached from this point of view.

From my own investigations, I am inclined to make a sharp distinction between the hereditary tremor of the type described by Dana and the motor disturbance which is here described as progressive dyssynergia. This is not a true tremor, but a synergic disturbance which is evident only when the extremity is in action, and consists of coarse irregular tremor-like movements in which the constant, vibratory characteristics of the true tremor is almost entirely lacking.

Furthermore, the cases of essential tremor which have come under observation during my investigations of this subject have failed to show the gradual mode of progression, and the associated symptoms of cerebellar disturbance which characterize the dyssynergia.

It may be well to emphasize the fact that in none of my cases of progressive cerebellar tremor was there any hereditary tendency or the slightest indication of tremor before the onset of the disease, which is so common a forerunner of the essential tremor neurosis.

CHAPTER IV.—THE RELATION OF THE SYMPTOMATOLOGY TO THE CEREBELLAR MECHANISM.

The more recent clinical and experimental studies of cerebellar function have shown very clearly that this organ, in addition to the role of maintaining equilibrium, plays an important part in the regulation and control of voluntary movements.

It is this function of the cerebellum which shows evidence of disturbance in *dyssynergia progressiva*. The absence of nystagmus, objective vertigo, cerebellar fits and disorders of the equilibrium would indicate that the structures subserving those functions are not affected.

The special influence which the cerebellum exercises upon voluntary movements is that of a controlling and reinforcing mechanism which is directly concerned with the regulation of tone, and the direction and measure of movements, the maintenance of attitudes, and the control of the synergies of co-ordinated movements. When these functions are disturbed there result the recognized classical symptoms of cerebellar origin; hypermetria, dysmetria, hypotonia, asthenia, cerebellar ataxia, volitional tremor and asynergia.

All modern authorities agree that the synergic function of the cerebellum is one of special importance. This is the faculty of accomplishing simultaneously and harmoniously the several movements concerned in a co-ordinated act. A disturbance of this function produces asynergia, which is so important a factor in the production of the cerebellar ataxia.

The cerebellar tremor, which is a volitional tremor, is also closely related to the loss of synergic control, and is regarded by most investigators in this field as an expression of asynergia. In other words, cerebellar tremor and cerebellar ataxia may be summed up as a cerebellar asynergia.

Babinski [1] has expressed this view in his brochure published in 1906, as follows:—

“The intention tremor which was first observed in multiple sclerosis is, according to all appearances, due to an alteration of the cerebellar mechanism. It may be explained by a defect in synergy among the different elementary movements of the upper extremity and more particularly in a disharmony in the function of antagonistic muscles.”

Stewart and Holmes [9], in a discussion of the symptomatology of cerebellar tumours, record the interesting fact in their remarks upon cerebellar ataxia that “in cases of chronic course, or when the lesion has become latent, the ataxia is as a rule less definite. Then it may be less typical and approximate to the intention type, characteristic of disseminated sclerosis.”

My own observations of the progressive cerebellar tremor fully confirm this point of view, namely, that intention tremor is essentially a disturbance of the synergies of muscles, and for this reason

the designation progressive cerebellar dyssynergia was chosen, as best expressing the true nature of the motor disturbance and its relation to the cerebellar mechanism.

If the symptomatology of the group of tremors under discussion is given careful consideration it becomes apparent that in all respects it is identical with the recognized symptomatology of cerebellar disease. There is the same hypermetria, dysmetria, hypotonia, asthenia, asynergia and tremor. All are present in their most exquisite form.

The exact localization of these functions in the cerebellar mechanism is still unknown. It can hardly be doubted, however, from recent experimental, anatomical and clinical investigations, that the cerebellar hemispheres (the "neo-cerebellum") are chiefly concerned with the regulation of the activities of voluntary movements.

Furthermore, the studies of Van Rynberk [8], Bárány [2], and Rothmann [7], have shown that there is a cortical representation in the cerebellar hemispheres, not only of the extremities but also, in all probability, their individual segments and articulations; so that the existence of cerebellar cortical centres for the control of co-ordinated movements is by no means improbable. If these results are confirmed, we have here represented the cortical mechanism for the control of voluntary movements, the loss of which results in these various motor disturbances of cerebellar disease.

In dyssynergia cerebellaris progressiva the clinical symptoms would indicate a progressive disease of that portion of the cerebellar mechanism which is engaged in the regulation of the tone, measure and synergies of co-ordinative movements. It begins gradually, and in the manner of an organic degenerative affection slowly affects the entire mechanism of the cerebellum. Apart from this, there are no other symptoms, the clinical picture is one simply of more or less generalized dyssynergia. For these reasons I believe that in this affection we have to do with a progressive degeneration of certain specialized cell or fibre systems of the cerebellar mechanism, the exact localization of which must await the results of pathological investigation.

SUMMARY.

The results of my investigations may be summarized as follows:—

There exists a chronic progressive form of cerebellar tremor, the most striking and characteristic symptom of which is a generalized volitional tremor which begins locally and gradually progresses.

In its advanced stage the disorder of motility is comparable in severity and violence with that of Huntington's chorea or the generalized athetosis. There is, however, this difference, that in a position of rest and muscular relaxation the tremor movements cease.

An analysis of the motor disorder show a marked disturbance of the ability properly to control and regulate co-ordinated movements. This is shown by the presence of hypermetria, dysmetria, adiadokokinesis, dyssynergia, hypotonia, and intermittent asthenia.

All of these symptoms, including the volitional tremor, coincide with the classical symptomatology which results from a loss of the cerebellar control over voluntary movements. The disorder is, therefore, regarded as of cerebellar origin.

The local onset, gradual progression, and chronic course indicate a progressive degeneration of certain special structures of the cerebellar mechanism presiding over the control and regulation of muscle movements.

Other symptoms of cerebellar disease, such as disturbances of equilibrium, objective vertigo, nystagmus, cerebellar fits and seizures are absent. For this chronic progressive disorder of the cerebellar mechanism the name *dyssynergia cerebellaris progressiva* is suggested as best indicating the essential element in the motor disturbance (dyssynergia), its progressive tendency and relation to the cerebellum. The chronic progressive cerebellar tremor is, however, equally descriptive and may be found preferable.

REFERENCES.

- [1] BABINSKI. "Synergie et inertie cérébelleuse," *Soc. de Neurol.*, July 5, 1906. (See *Archives de Neurol.*, 1906, t. xxii, p. 48.)
- [2] BÁRÁNY. *Wien. klin. Wochenschr.*, 1912, Bd. xxv, S. 2033.
- [3] DANA. "Hereditary Tremor: a hitherto undescribed form of motor neurosis," *Amer. Journ. Med. Sci.*, 1887, xciv, p. 386.
- [4] FLATAU. "Ueber hereditärem essentiellen Tremor," *Arch. f. Psych.*, 1908, Bd. xlv, S. 306.
- [5] GRAUPNER. "Hereditärem Tremor," *Deutsche Arch. f. klin. Med.*, 1899, Bd. lxiv, S. 466.
- [6] MINKOWSKI. "Ein Fall von hereditärem Tremor," *Münch. med. Wochenschr.*, 1901, Bd. xlviii, S. 607.
- [7] ROTHMANN. *Berl. Gesellsch. f. Psych. u. Nerv. Krank.*, March 14, 1910. (See *Berl. klin. Wochenschr.*, 1910, Bd. xlvii, S. 1035.)
- [8] VAN RYNBERK. *Folia Neurobiologica*, 1908, Bd. i, S. 403.
- [9] STEWART, GRAINGER, and HOLMES, GORDON. "Symptomatology of Cerebellar Tumours," *Brain*, 1904, vol. xxvii, p. 534.

THE PHYSIOLOGICAL SIGNIFICANCE OF THE REFLEX PHENOMENA IN SPASTIC PARALYSIS OF THE LOWER LIMBS.

By F. M. R. WALSH, M.D., B.Sc., M.R.C.P.

Resident Medical Officer to the National Hospital, Queen Square.

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INTRODUCTION.

WHILE the destruction of pyramidal fibres is universally accepted as an adequate explanation of the loss of voluntary power in spastic paralysis, there is still much discussion as to the cause of the other phenomena that are constantly present, namely the hypertonus of the muscles, the exaggeration of the tendon-jerks and the reflex movements that occur.

The original view of Charcot, who regarded spasticity as an

irritation phenomenon, has been universally discarded as plainly untenable, while the illuminating and philosophical conceptions of Hughlings Jackson, to which I shall later have occasion to refer in detail, have not received from modern workers the appreciation or comprehension they would seem to demand if the problems of spastic paralysis are to be solved.

To the German school of neurologists we owe a great number of recent researches into the phenomena of spastic paralysis. Prominent among these are the contributions of Foerster [20], v. Monakow [32], and Rothmann [35]. The hypotheses put forward by these authors deal with hypertonus and contracture rather than with reflex movement. To the French school of neurologists, mainly, we owe our knowledge of the striking reflex movements that occur in the lower limbs in cases of spastic paralysis, but, until quite recently, there has been no attempt to elucidate the physiological significance of these, and it is within the last few years only that, in the work of Marie and Foix, we find a departure among French writers from the merely clinical description of phenomena that have been studied since the days of Charcot.

Although the two last authors have thrown considerable light on the nature of these reflex movements, there is still to be attempted any real effort to correlate them with the other features of spastic paralysis; and it still remains true that many of the phenomena of spastic paralysis are obscure and problematic in origin, and many clinical observations on this subject have yet to find their place in any body of physiological theory. Further, the masterly work of Sherrington has not received from clinicians the attention it merits, and with the exception of two papers of recent date by Marie and Foix has not inspired any clinical work of note; no broad attempt has been made to correlate the physiological findings of Sherrington in animals with the phenomena observed in man in certain conditions of disease of the nervous system.

The observations recorded in this paper have been made with this end in view, and a special study, therefore, of the phenomena of spasticity, contracture, exaggeration of the tendon-jerks and of reflex movements has been made. It is proposed in this present paper to give the results of detailed examination of the reflex movements found in the lower limbs in a large number of cases of spastic paralysis of all kinds, special attention being given to the relation between these and the other above-mentioned features of spastic paralysis. In a subsequent paper it is hoped to deal with the kindred phenomena of hypertonus and contracture.

I wish here to express my indebtedness to the medical staff of the National Hospital for permission to record the results of my examination of cases in the Hospital practice, and to Dr. Hood for placing at my disposal the patients under his care in the St. Marylebone Infirmary. To Dr. Gordon Holmes I am deeply indebted for much advice and assistance.

CHAPTER I.—HISTORICAL.

The reflex movements of the lower limbs in spastic paralysis have long been familiar to neurologists. They include the common involuntary flexor spasms seen in many cases of paraplegia, and the reflex movements occurring on stimulation of the limb, the "*Abwehrbeugereflexe*" of German authors, the "*Réflexes cutanés de défense*" of Babinski. We must add to these the more recently described "extensor response"; Babinski's "*Phénomène des orteils*."

It is not generally recorded in references to the earlier views on the causation of the "positive symptoms" (Jackson [25]) of spastic paralysis, namely the spasticity and reflex augmentation, that Charcot [13] taught that there were two factors responsible for the appearance of these, "the suppression of the moderator influence of the brain, and probably, also, the irritation of which the grey substance, in its turn, becomes the seat."

In regard to the inhibitory function of the pyramidal system Foerster [21] considers the removal of this function is the primary cause of spasticity. When it fails, "the unimpeded sensory afflux charges more and more the anterior horn cell, increases its excitability, and produces a permanent motor stream from the ganglion-cell to the muscle, that is to say, the spastic contracture." To explain the associated reflex movements [22] he assumes that the cerebral control over lower motor mechanisms being lost, the limbs come again under the influence of certain phylogenetically old subcortical motor centres, which determine an attitude of flexion of all the limbs, a "subcortical fixation reflex." Our ancestors, he assumes, were climbing animals, and as such used the flexors to a greater extent than other muscles. In the new conditions, these react more readily to peripheral irritation, and hence we see, for example, the well-known flexor spasms of spastic paraplegia.

V. Monakow [32] and Rothmann [35], although they do not believe in the inhibitory function of the pyramidal tract, agree with

Foerster in ascribing to extrapyramidal subcortical motor systems an important rôle in the causation of spasticity and reflex phenomena.

Babinski regards the reflex movements as defensive in nature. Marie and Foix [30] regard all the reflexes of the spastic lower limb as evidence of spinal function liberated from cerebral control. They accordingly describe them as "Réflexes d'automatisme médullaire."

These authors, and later Strohl [39], describe reflex flexion of the limb as occurring invariably on stimulation of its skin or deep structures, except in a few cases where stimulation of the proximal parts of the limb gives reflex extension. Moreover this flexion is often accompanied by simultaneous extension of the opposite limb. They conclude that these reflex movements of the lower limb represent the mechanism of locomotion, a spinal function liberated from higher control by a lesion of central descending paths. They consider that the movements they have seen clinically in man are analogous with the "spinal stepping" of animals described by Sherrington [37]. They find that the Babinski type of plantar reflex is elicited by the same type of stimulus as reflex flexion of the limb, and they regard it as the minimal motor reflex response of the limb. Babinski, on the other hand, says that the pathological plantar response and the "defence reflexes" are separate phenomena [8].

Whether this be so or not, there can be no doubt that the work of Sherrington [36] throws a new light on the phenomena of spastic paralysis. In his studies on the physiology of the nervous system, he has used decerebrate and spinal animals. These differ in that the former shows a maintained tonus of the extensor muscles of the limbs, that is, of the muscles maintaining the animal in the erect posture, while the spinal animal has not this tonus. Among the reflex movements found in these animals are some of protective nature and others subserving the function of locomotion, and the fact of such great significance for the study of spastic paralysis is that Sherrington has revealed the existence of two reflex systems in the brain-stem and in the cord, each governing its own group of muscles and giving rise to reflex reactions peculiar to itself.

One reflex system employs the extensor muscles of the limbs. These are engaged in a *static* reflex; that is, the reflex which they subserve determines a condition of *tonus* in them. This Sherrington regards as the expression of posture [38]. The centre governing this reflex has been shown to be higher than the cord, in the brain-stem, and section of the brain below the level of the pons abolishes this reflex tone.

The other reflex system employs the limb flexors. The reflex reactions of this system are characteristically *phasic*, or clonic, in nature. They give rise to reflex *movements*. In the decerebrate animal both systems are in activity, in the spinal animal the static reflex of posture is absent and we see the phasic, spinal reflex system alone active. We have, therefore, two physiological groups of muscles, each engaged in a type of reflex reaction peculiar to itself. The nervous mechanisms of these are differently represented in the nervous system, the tonic extensor system requiring the presence of a "prespinal" centre, the phasic flexor system being purely spinal. One of the most striking reflexes described by Sherrington is the flexion reflex of the hind limb [37]. This consists of a single flexion, or withdrawal, of the limb in response to nocuous stimuli applied to any part of the limb surface, to any of its deep structures, or to any afferent nerve of the limb. This reflex flexion is constant except in the case of stimuli applied to the attached base of the limb, where reflex extension is often evoked. The flexion reflex is at times accompanied by synchronous extension of the contralateral limb. It is protective in function. "Spinal stepping" is also obtained from such animal preparations, but by a totally different type of stimulus.

Surely these physiological facts must have some value in the elucidation of pathological conditions in man. Sherrington [36] says: "Just as certain agents" (strychnine and tetanus toxin) "display their action more obviously in one member of these paired systems than in the other, so processes of disease may be expected to deal with the two systems unequally, and to reveal more obviously and affect more deeply one of them than the other."

It is here that we must pay tribute to the genius of Hughlings Jackson [25]. In speaking of the rigidity in hemiplegia, he says: "My speculation is that the rigidity is owing to unantagonized influence of the cerebellum. I believe that in health the whole of the muscles of the body are doubly innervated, both by the cerebrum and the cerebellum, there being a co-operation of antagonism betwixt the two great centres. Whilst the cerebrum innervates the muscles in the order of their action from the most voluntary movements (limbs) to the most automatic (trunk), the cerebellum innervates them in the opposite order. This is also supposed to be the order of their degree of influence on parts, and is equivalent to saying that the cerebellum is the centre for continuous movements and the cerebrum for changing movements."

"The muscles which, on the above suggestions, are chiefly innervated

by the cerebellum are those which have the fewest different, the most tonic, the most confluent movements, the reverse for those which the cerebrum chiefly innervates. Thus, in walking the cerebellum preserves the equilibrium of the body, tends to stiffen all the muscles; the changing movements of walking are the result of cerebral discharges overcoming in a particular and orderly way the otherwise continuous cerebellar influence. This is what is meant by a co-operation of antagonism." This quotation at length demands no apology, so significant is this hypothesis in view of Sherrington's work. The existence of a double system of motor innervation, so ably foreshadowed by Jackson, has actually been demonstrated in animals. That recent work has shown that the cerebellum itself is not the seat of the functions which Jackson assigned to it, is of minor importance; the significant fact is that he believed in the existence of two systems of motor innervation, each acting on its own group of muscles in a manner peculiar to itself and giving rise to reactions of two different types, tonic and clonic. Moreover, he recognized that disease could affect these systems separately.

CHAPTER II.—METHODS OF INVESTIGATION.

In man it is not possible to analyse reflex movements with the detailed accuracy possible in animal experiments, in which Sherrington [37] has been able to isolate and expose individual muscles, thus ascertaining the part each plays in a given reflex. We have to be content with the method of inspection to reveal reflex movement, and in the case of reflex muscular contraction without movement, palpation is the only method available. However, by means of graphic methods it has been found possible to obtain permanent records of certain reflex movements, in which the time relations and the form of the movements are seen (see Appendix II).

The clinical examination of the reflexes necessitates a study of the following points; the attitude of the limb as the patient lies in the dorsal position in bed, the voluntary power, the muscle-tone and the relative distribution of these in the different muscle groups, and the type of contracture present.

The condition of the tendon-jerks also demands attention, and in addition to the ordinary method of eliciting the knee-jerk, a quadriceps-jerk may be sought by percussion over the heads of the metatarsals

on the sole. This area has been described by Cohn and Loewy [28] as the "reflexogenous plantar zone of quadriceps." According to these authors, it yields on percussion a quadriceps-jerk in conditions of increased tonus, but I shall show that the response varies according to the type of stimulus and according to the facility of the reflex flexion in the limb. The knee- and ankle-jerks are regarded in this paper as a measure of the state of tone in the *extensor* muscles of the limb, and in these alone.

The *hamstring-jerks* obtained by percussion of the tendons of semitendinosus, semimembranosus and biceps femoris are not mentioned in the extensive literature devoted to the subject. They are best elicited by laying the index finger across the tendons at their insertions and then percussing the finger. In this way the muscular contraction is readily felt when direct observation is prevented by obesity and other causes. There can be no doubt that the muscular contractions obtained in this way are true tendon-jerks and are not due to direct mechanical excitation of the muscle-fibres, since in *tabes*, in which mechanical excitability is preserved but the tendon-jerks are abolished, these hamstring phenomena are absent too. They afford evidence of the state of tone in the limb *flexors*.

In observations on the reflex movements it is essential to record the site and nature of the stimulus evoking the reflex and the characters of the reflex motor response; that is, the muscles which contract and the order in which their contractions appear. The influence of initial posture on the form of the reflex movement and the presence or absence of reflex movement in the opposite limb also require attention, and finally the relation between the type of reflex present and the distribution of tone and power in the muscles of the affected limb is of the utmost significance.

The detailed study in the investigation on which this paper is based of a large series of cases of spastic paralysis of all kinds, sixty cases of spinal lesion and twenty of cerebral lesion, has given certain constant findings, which justify very definite conclusions as to the nature and cause of the reflex phenomena of the lower limbs. These present the closest possible analogies with the reflexes described by Sherrington in animals under experimental conditions, and there is, as will be shown, strong evidence of the existence in man of the two reflex systems found in the brain-stem and in the cord of animals.

CHAPTER III.—THE FLEXION REFLEX.

The most frequent and constant reflex movement occurring in the lower limb is that of flexion. I shall speak of this as the flexion reflex. It can be obtained by a wide range of stimuli, cutaneous and deep. The movement takes place at all joints and is very constant in form, varying in amplitude alone according to the conditions of stimulus. It is also seen in the spontaneous flexor spasms of many cases of spastic paraplegia.

A complete flexion reflex consists of a single flexion at hip and knee with dorsiflexion of foot and toes, and the flexion is steadily maintained during the application of the stimulus and is not alternating in character.

Direct examination reveals contraction in the following muscles in this reflex; tensor fasciæ femoris, rectus femoris, semitendinosus, semimembranosus, biceps femoris, adductor longus, extensor longus hallucis, tibialis anticus, and extensor longus digitorum. In certain conditions there is also contraction of the peronei, but this is not an essential part of the reflex response. Probably other muscles are involved, e.g., iliopsoas and pectineus, but under clinical conditions complete analysis of reflex movement is not possible, since we are limited to inspection and palpation as means of investigation.

When the reflex is fully developed, whatever be the intensity of the motor response, these muscles all contract, even though the contraction may not be sufficient to cause movement. As is the case with the flexion reflex of the spinal animal, a strong reflex differs from a weak one, not in the number of muscles involved, but in the force of contraction in them. In certain conditions, however, such as "spinal shock," this is not strictly true, and the threshold of stimulation of the different muscles does vary to a limited extent.

The flexion may not, in certain cases to be considered later, be maintained at a uniformly high level and then gives the appearance of alternating flexion and extension, but no true alternation occurs and the flexion reflex of the limb is a single flexion of the limb at all joints varying in duration with the duration of the stimulus (see p. 300).

This reflex flexion of the limb I shall speak of as *the flexion reflex of the lower limb*, and I now proceed to study it in detail. Certain other reflexes, however, also occur, such as crossed extension and homolateral extension; these will be dealt with in turn.

It may be pointed out that homolateral reflex extension is an

unusual phenomenon, and that, as a general rule, admitting of but rare exceptions, sensory stimulation of a spastic leg evokes reflex flexion as "end effect."

§ 1.—*The Receptive Field of the Reflex.*

Sherrington has named the total area from which a reflex may be elicited, the receptive field for the reflex.¹ In the reflex under consideration in man this is very extensive, and when typical includes the skin and deep structures of almost the entire limb. The reflex is most readily obtained from the sole, the distal extremity of the limb, and here the threshold of stimulation is lowest. When reflex activity is considerably lessened, as after a complete transverse lesion of the cord, or in the coma preceding death, the field is confined to the sole and no reflex response can be obtained from any other part of the limb.

When the reflex is well developed, cutaneous stimuli applied to any part of the limb surface, and even to the lower part of the abdominal wall, will elicit a reflex complete in form. However, as we recede from the free extremity of the limb, the threshold of stimulation rises, and stronger and more prolonged stimuli are needed to evoke any response.

In certain rare cases stimulation of the skin of the upper fourth of the thigh and of the perineum gives reflex extension as end effect. When this occurs I have sometimes found that there is an intermediate zone of skin where stimulation gives either extension or flexion, or extension followed by flexion, and figs. 2, 3 and 4 are from such a case.

Since also, as will be shown, the reflex can be obtained by stimulation of deep structures, the field includes the whole structure of the limb up to a certain level. In an average reflex the field extends up to the upper fourth of the thigh, but it may extend to the abdomen, or be limited to the sole.

When any crossed reflex accompanies it, the field of this is the same as that of the homolateral flexion reflex.

Within the area of the receptive field reflex flexion is invariably obtained on adequate stimulation, but certain minor differences in this flexion are seen according to the site of the stimulus. These differences in the motor response may be described as the "local sign" of the reflex in question, and they consist in a relative predominance of the contraction in certain of the muscles involved.

I have mentioned that in conditions of "shock" of the central

¹ In describing the reflex phenomena here dealt with I use wherever applicable the terminology introduced by Sherrington in his studies on reflex action in animals.

nervous system, as in cases of acute or complete transverse myelitis, or in the coma preceding death, and also in certain cases of hemiplegia, the area from which the reflex can be elicited is restricted to the sole.

The following case of acute transverse myelitis at the ninth dorsal segmental level illustrates this :—

M. W.—A complete paraplegia of sudden onset and of twelve months' duration. There was absolute motor and sensory loss below the umbilicus, with general wasting and bed sores. The lower limbs were flaccid and all the tendon-jerks absent. According to the theory of Bastian, the condition was one of complete physiological transverse lesion of the cord.

Light stroking of the sole was without effect, but heavy stroking with the end of a penholder gave a typical "extensor response" with just perceptible flexion at hip and knee. Pin-prick gave a brisk reflex response from the sole and the outer edge of the foot. Tarsus compression gave a very feeble response. No form of stimulus applied at a higher level gave any reflex response.

The same state of affairs is found in cases of spastic paralysis immediately before death. As the reflex activity of the limb lessens, the reflexogenous area becomes smaller, but until an hour or so before death a reflex response is obtainable from the sole. *We may regard the sole, therefore, as the most essential part of the receptive field.* The importance of this will be apparent when we discuss the functional significance of the flexion reflex.

Babinski [1], however, first drew attention to the fact with which all neurologists are familiar, that stimulation of the inner border of the sole often gives a normal plantar reflex—a flexor response—while if the outer border of the sole be stimulated the extensor response is seen.

This would seem to negative the view here advanced as to the extent and character of the receptive field. My observations have led me to regard this contradiction as apparent only.

It has to be remembered that the area of skin from which the plantarflexion of the hallux is obtained in these cases overlies the abductor hallucis muscle and that the plantar fascia here is thin. A strong mechanical stimulus here produces plantarflexion of the hallux by direct stimulation of this muscle, the contraction of which flexes the hallux.

Simple localized pressure, as with the end of a penholder, over this muscle will give a plantarflexion of the great toe, while applied elsewhere to the sole it gives no response. As remarked in another

part of the paper, *localized* pressure of this type does not commonly elicit any reflex response, and it seems therefore highly probable that in many cases this toe phenomenon is not a true reflex, but purely local.

In other cases where this explanation has not been found to apply, the phenomenon seems always due to the fact that the field is restricted to the outer fraction of the sole. This is often the case in hemiplegia, where this double phenomenon is most common.

§ 2.—*The Nature of the Stimulus.*

Light touch, such as the contact of cotton-wool, or of a camel's-hair brush, except in very rare instances gives no reflex response. I have only seen it thus obtained twice in the whole series of cases examined, and in these the reflex was very facile.

Light pressure to the sole, applied, not as a contact but as a stroking movement, gives in typical cases a good reflex response. This is the method in common use in eliciting the plantar reflex, and if the stimulus be gentle a dorsiflexion of the hallux may be the only visible effect, but this is never the only muscular contraction, and palpation of the hamstring tendons reveals, even to minimal stimuli, contraction of these muscles.

This type of stimulus is commonly effective in evoking a reflex response when applied to the sole and the outer half of the dorsum of the foot as high as the lower end of the external malleolus. When very facile the reflex is elicited by each stroke to the skin over this area. The threshold is lowest on the outer border of the sole and at the base of the hallux. At higher levels on the limb cutaneous stimuli of this type are commonly ineffectual.

Nocuous stimuli, that is, stimuli normally painful, such as pin-prick or pinching of the skin, give a good reflex over the whole receptive field, the upper limits of which indeed are defined by the use of such stimuli. Above the level of the foot, however, repeated stimuli of whatever form are often needed to elicit a response, and they have to be correspondingly stronger the further they are removed from the extremity of the limb. Usually on the sole and dorsum a single pin-prick gives quick ample flexion, while on the thigh several stimuli delivered in quick succession may be necessary.

Stimulation of the deep structures of the limb gives a reflex identical with that obtained by the methods mentioned, above. Applied to

muscles and tendons we find, as in the case of cutaneous stimuli, that stimulation of distally placed structures gives a readier response than that of proximal muscles, &c. When the receptive field is limited we find that while, for example, pinching of the tendo Achillis gives a flexion reflex, Oppenheim's procedure may be ineffectual, or that when this latter gives a reflex, pressure of the thigh muscles may be inadequate. I have only twice been able to satisfy myself that Oppenheim's procedure will elicit a reflex when all forms of equally intense cutaneous stimulation to the foot fail to do so.

Forcible compression of the tarsus and forced flexion of the toes, as practised by the French observers, are examples of stimulation of joints and muscles which give reflex flexion of the limb.

Electrical stimuli, such as the faradic current, or thermal stimuli, are equally effective in giving a reflex movement when applied to the receptive field.

The reflex contraction of quadriceps extensor femoris mentioned earlier (Loewy [28]) is an instance of a single form of stimulus, namely, a sudden localized light pressure, giving a specific motor response from a certain skin area. I have found in cases of spastic paraplegia, that where a light tap on the sole gives this movement, a heavier tap gives reflex knee extension followed by a typical complete flexion reflex; a harmless stimulus gives reflex extension, a more intense, nocuous stimulus gives also reflex flexion—or this alone.

Sherrington [36] describes a similar phenomenon in the spinal dog, in the "extensor thrust" reflex, where light pressure between the toe pads gives a reflex extensor thrust of the limb, but all other forms of stimulation, thermal, painful, or electrical, give a flexion reflex.

In cases of paraplegia with contracture in flexion where involuntary flexor spasms occur, the lightest stimulation applied to any part of the limb, even contact with moving bedclothes, gives reflex flexion; and it is in such cases alone that passive movement is an adequate form of stimulus. In these cases, any attempt to straighten the partially flexed limb provokes strong reflex flexion at hip and knee with dorsiflexion of foot and hallux.

In limbs only moderately spastic, or spastic in extension, passive movement alone gives no reflex response.

Many patients were supported astride a horizontal bar with the legs hanging free. The passively flexed limb was suddenly released and allowed to fall into extension, but no reflex flexion, or any form of reflex whatever, was to be obtained.

In conclusion, when the reflex is present it can be elicited by stimulation of various forms applied to any part of the limb, except part of its proximal extremity. Although light and painless stimuli applied to the free extremity of the limb give the reflex, yet it is most characteristically obtained by stimuli which are harmful in character, or nocuous. The two types of reflex obtained from the sole by percussion exemplify the importance of the nature of stimulus in determining reflex response, but with this exception any stimulation when applied within the receptive field gives reflex flexion as its motor effect. The threshold is lowest at the distal extremity of the limb and here alone light stimuli are effective.

§ 3.—*The Motor Reflex Response. The "Extensor Plantar Response."*

I have said above that all the flexors of the limb are activated in the flexion reflex. These include hip and knee flexors and the dorsiflexors of the ankle and digits. Now, of these, the dorsiflexors, in anatomical nomenclature, are named extensors. There can be no doubt, however, that these muscles must be grouped physiologically with the flexors.

In involuntary flexor spasms and in the flexion reflex elicited as already described these muscles act with the flexors of hip and knee, while with reflex extension we always see plantarflexion of foot and digits. Of the general shortening of the limb, which occurs in the flexion reflex, dorsiflexion is the natural accompaniment.

Moreover, the lower limb of man can be compared, segment for segment, with the hind limb of the dog, and Sherrington has shown that here the dorsiflexors act with the flexors and must be regarded as such, while plantarflexion and extension at hip and knee are, on the other hand, similarly allied.

The following comparative diagram (fig. 1) shows this: A is the hind leg of the dog, and B the lower limb of man. A is after Sherrington [37].

The flexors therefore are: Ilio psoas, rectus femoris, sartorius, gracilis, pectineus, adductor longus and brevis, tensor fasciæ femoris, semitendinosus, semimembranosus, biceps femoris, tibialis anticus, extensor longus digitorum, extensor longus hallucis. These are not all represented in the diagram.

With the methods at our disposal in clinical investigation, it is not easy completely to analyse any complex reflex movement. For example, slight contraction of sartorius or rectus femoris may easily

pass unobserved. On the other hand, the slightest twitch of tensor fasciæ femoris is at once visible, while palpation of their tendons reveals the slightest contraction in the hamstring muscles.

Certain muscular contractions, therefore, are not seen. In the case of the toes, however, where the effect of gravity is negligible, as it cannot be in the case of more proximal joints, a hallux movement betrays the least contraction of the extensor longus hallux. In a feeble

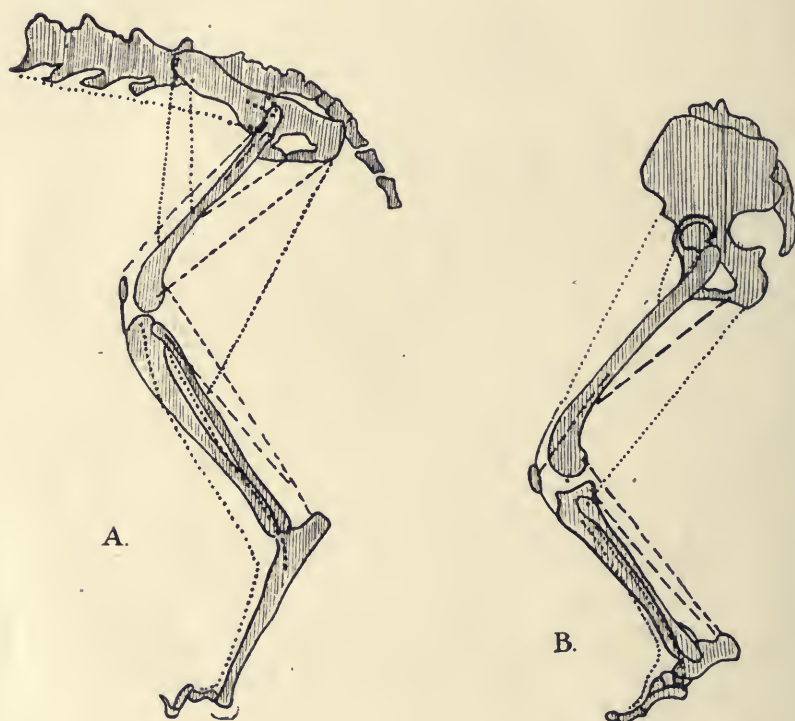


FIG. 1.—In A, the muscles activated in the flexion reflex of the hind limb of the spinal animal are indicated by dotted lines; their antagonists by interrupted lines. In B, the muscles acting in the flexion reflex are similarly indicated.

reflex this may be the only *visible* effect, but it is by no means the only one present, and careful investigation has drawn me to the conclusion that an isolated “*extensor response*” does not occur. It is invariably accompanied by contraction of the proximal flexors of the limb, and in all cases a palpable contraction of semitendinosus and semimembranosus can be felt, while in a majority where the reflex is well developed an actual movement of flexion at hip and knee obtains. The importance

of this fact in any attempt at analysis of the nature of the "extensor" type of plantar response will be at once apparent.

We know also that the flexion reflex is most readily elicited from the sole and that here light stimuli, such as are adopted to elicit a plantar reflex, suffice to give it. It becomes evident, therefore, that the "extensor response" has, in common with the flexion reflex, its site and mode of stimulation and its form, and there is no doubt that this well recognized and important sign of pyramidal lesion is part of the flexion reflex. It may be said at once that Babinski [8] refuses to accept such an interpretation, which Marie and Foix [30] have already put forward in a somewhat qualified and different form.

It might be thought, as these authors say, that the "extensor response" is the minimal response or "motor focus" of the reflex. This is not always a point easy of solution, since, as I have pointed out, the contractions of certain proximal flexors are not easy to observe and do not lend themselves to graphic recording as readily as toe movement.

A study, however, of the reflex in conditions of "spinal shock" shows that the inner hamstrings are the muscles which are earliest involved and form the "motor focus" of the reflex.

From this point of view, observations were made on three patients with hemiplegia from cerebral tumour, when comatose and at the point of death. The affected limbs became absolutely flaccid, and the tendon jerks disappeared while a flexion reflex remained still readily obtainable from a fairly wide receptive field on intense stimulation, such as pinprick or pinching. Gradually the field became smaller until from the sole alone could a reflex be elicited. In all three instances the following phenomenon was then seen: The reflex motor response became less ample and forcible until only a toe movement was seen, but a palpable hamstring contraction remained, and in one of the three, an emaciated patient, this indeed could be seen. The field of musculature involved then shrank until the toe movement went, and the only evidence of reflex response on stroking the sole was a readily felt hamstring contraction. Finally, this went and the limb retained no sign of reflex action.

I think it justified, therefore, to regard these muscles, in man as in animals according to Sherrington, as the motor focus of the reflex. It must be admitted, though, that certain deep-lying proximal flexors could not be investigated.

Case 1 (in the Appendix) shows this phenomenon inversely. It was a case of acute complete transverse myelitis. When seen a week after

onset there was absolute flaccid paralysis with retention of urine, complete sensory loss over the lower limbs and absent tendon-jerks; judged by Bastian's criteria, a total tranverse lesion.

Heavy stroking of the sole, and here only, gave reflex flexion at hip and knee, feeble but definite. There was no foot or toe movement. The minimal motor response was hamstring contraction alone.

Within the next few days the reflex response increased, dorsiflexion of foot and finally of hallux appearing. From this time on an "extensor response" could be obtained, but hamstring contraction still remained the minimal motor response to slight sole stimulation.

Here we can see the variation in threshold of contraction of the different muscles, a variation which is not evident in the fully developed reflex. The muscles disappear from the reflex response in the inverse order to that in which their contractions first appear.

The "extensor plantar response" is therefore not the minimal motor response, and it is never obtained without contraction probably of all the limb flexors, certainly of some proximal flexors. *It is not separable from the flexion reflex.*

Is limb flexion ever associated with plantarflexion of foot and toes, i.e., with a so-called "flexor response"? This question brings us to the consideration of "local sign" in reflex response.

It has been shown that within the limits of the receptive field an adequate stimulus gives only one type of reflex response, namely flexion of the limb. Yet it was long ago pointed out by Babinski [1] that the pathological type of plantar reflex varies somewhat in form according to the site stimulated. He observed that stimulation of the outer border of the sole gave eversion of the foot as well as the toe movement, while from the inner border of the sole inversion of the foot occurred. Further he says that, in some instances, limb flexion when elicited from the thigh is accompanied by plantarflexion of the toes—a "flexor response" [8].

It is found that when the flexion reflex is present, dorsiflexion of the hallux always results from stimulation of the sole, and is accompanied by contraction, more or less forcible, of the limb flexors. Stimulation of the upper limits of the field gives the same type of reflex, but certain modifications are sometimes present. These are that the contraction of the distal muscles is less powerful, and there may be little, if any, "extensor response" in such cases, which, however, are the exception. In two of the instances in which I have observed slight actual plantarflexion accompanying limb flexion, this was not an active

movement but a passive pull when the foot dorsiflexed, since if the dorsiflexion of the foot was prevented and the angle between foot and leg maintained constant, this movement did not occur.

In another class of case active plantarflexion does occur (*see* figs. 2 and 3), but graphic records show that it precedes a dorsiflexion movement which synchronizes with the limb flexion.

In a case of this type, which was one of syphilitic focal myelitis with spasticity in extension, exaggerated tendon-jerks, clonus and Babinski type of plantar reflex, pinching of the skin of the thigh gave the

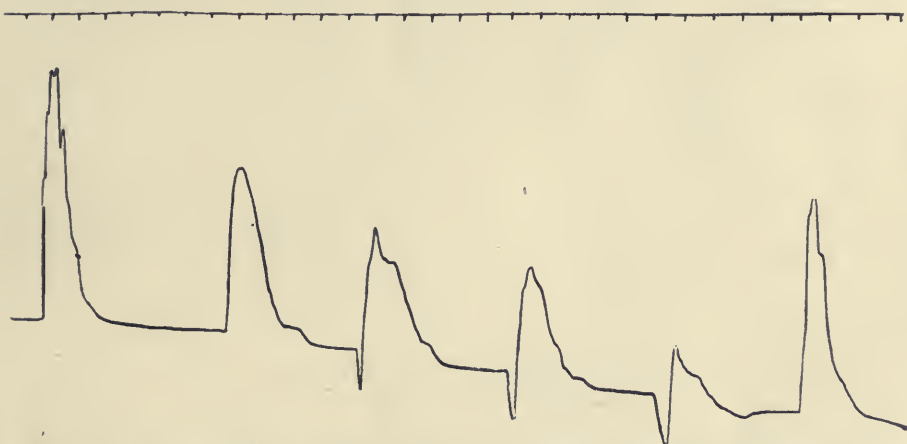


FIG. 2.—Records a series of hallux movements obtained by stimulation of the skin of the limb. An upward movement is one of dorsiflexion, and a downward excursion represents plantarflexion. Six stimuli were applied in rhythmic succession; the first and last to the sole, the others consisted of pinching the skin on the inner surface of the thigh. Sole stimulation gave a pure "extensor response." Of the thigh stimuli, the first gave simple dorsiflexion. The others gave always plantarflexion, a "flexor response," followed by an "extensor response" (time in seconds).

following results. The first stimulus gave invariably a pure flexion reflex with an "extensor" plantar response. Subsequent stimuli, however, in a rhythmic series, gave a plantarflexion of toe and foot followed by limb flexion including foot and toe dorsiflexion (fig. 2). The whole movement was so brisk as to leave the impression that the reflex movement consisted of a "flexor response" and limb flexion. The records (figs. 3 and 4) prove that this is not so and demonstrate the identity of the "extensor" type of reflex response with the flexion reflex.

In this case, stimulation of the skin of the perineum gave reflex extension of the limb with plantarflexion of foot and toe, and there was,

therefore, a transitional zone from which, on stimulation, there was obtained a reflex extension followed by a reflex flexion.

A third class of case, in which this anomaly may appear, is in old-standing paraplegias with contracture of the toes in plantarflexion. In such a case a dorsiflexion of toes is impossible. It would be superfluous to emphasize this were it not that such a case has been used by Babinski [8] to prove that these two phenomena of limb flexion are separable and different in nature.

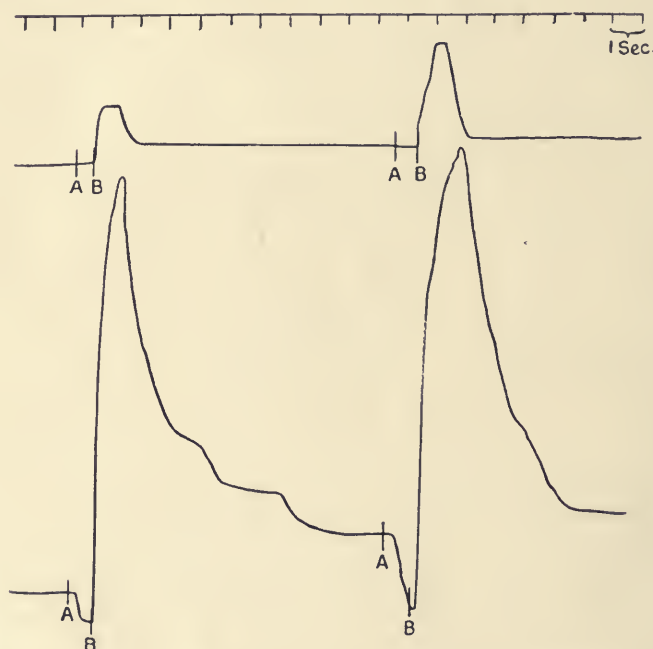


FIG. 3.—Simultaneous comparative records of toe movement and limb flexion at hip and knee. The upper tracing records only limb flexion, and was taken from the external malleolus. The lower, taken from the tip of the hallux, records the plantar reflex also. The vertical strokes (A and B) through the records indicates corresponding places in the two cases. The stimulation was in each instance a pinch of the skin on the inner side of the thigh (upward movement = dorsiflexion). These show that the "flexor response" consists of a feeble plantarflexion of hallux, which precedes the ample dorsiflexion of foot and toe, this latter being synchronous with the limb flexion of which it is a part.

The consideration of these cases in which plantarflexion of foot and toes is associated with limb flexion, raises the question of the relationship between the normal "flexor response" and limb flexion as a whole. I shall later refer to some of the characteristics of the normal plantar response in detailing the differences which exist between it and the

crossed plantar reflex. The normal plantar reflex, as I shall there describe it, consists of plantarflexion of digits, and is accompanied by dorsiflexion of the foot, contraction of tensor fasciæ femoris, and certain other variable contractions of the limb musculature.

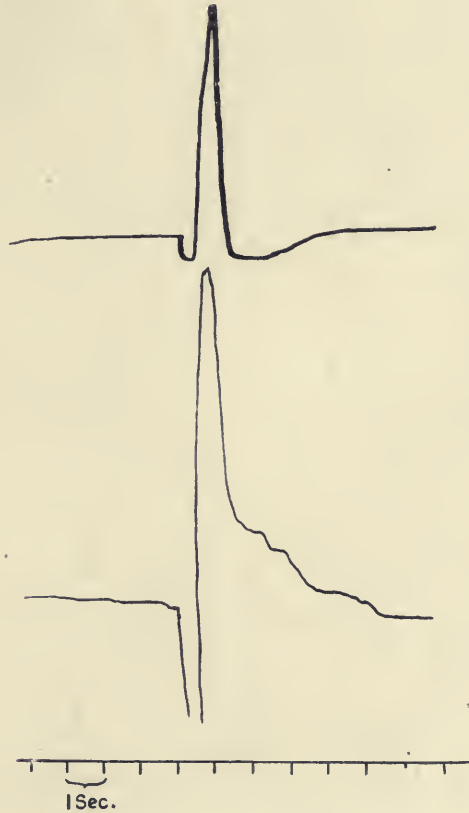


FIG. 4.—Synchronous records of hallux and foot movement in a diphasic response, such as those in figs. 2 and 3. The upper was taken from the ball of the foot by means of a thread connected with a writing lever. The lower tracing was similarly taken from the tip of the hallux. They show that in the preliminary plantarflexion, both toe and foot take part, just as in the subsequent “extensor response.” In each case the hallux movement is the more ample.

In some cases, apparently flexor and extensor movements are combined in varying proportions, so that, as far as my investigations go, the normal “flexor response” does not appear to form part of any systematic reflex movement of flexion, such as seems to be the case with the “extensor response.” It is open to question whether the normal plantar

reflex is a co-ordinated movement involving contraction and relaxation of opposing muscle groups, that is, "reciprocal innervation," such as the pathological reflex undoubtedly is.

§ 4.—*Involuntary Flexor Spasms and Paraplegia in Flexion.*

In this description of the reflex movement, I have so far dealt with a definite reflex elicited by a definite, known stimulus. What place do the involuntary flexor spasms, so prominent in some cases of spastic paraplegia, take?

Examination reveals that each flexor spasm is a powerful flexion reflex complete in form. These spasms occur most frequently in cases of paraplegia in flexion, and as the extended type of paraplegia passes on to this severer form, the flexor spasms increase in strength and frequency. Until Babinski drew attention to the flexed form of spastic paraplegia and showed that it possessed constant characteristics, it was the custom, and still is in this country, to dismiss it lightly as differing from the form in which the legs are extended, only by the presence of contracture in the flexors. But, as Babinski [5] has pointed out, this so-called "contracture" is an active muscular contraction, and permanent fibrous contracture is but a terminal phenomenon. Moreover, the condition is characterized by complete intermissions of the spasm, which result in the production of alternating flexion and extension movements. Of these the former are active, the latter generally passive and due to relaxation of the flexor spasm. Legs spastic in extension show no such variations.

In paraplegia in flexion we have a condition in which the extensor muscles show little or no trace of reflex action, and in which the flexors are, therefore, unantagonized. The intermissions described by Babinski are periods between successive flexor spasms, or flexion reflexes.

—Even when this condition of complete absence of reflex action in the extensors has ensued in a progressive paraplegia, the reflex activity of the flexors remains characteristically phasic, and a permanent attitude of the limb in flexion only appears when actual contracture has set in in the muscles. Palpation of the tendons of the hamstrings reveals the markedly intermittent nature of the spasms, and it is when these are minimal or absent that hamstring-jerks are to be obtained most readily.

Whether these flexor spasms are actually spontaneous or not is uncertain. Any manipulation of the limb, or any light cutaneous stimulus such as that of cold when the bedclothes are removed, increases the spasm. Also since we know that an intact afferent path from

muscles to cord is essential (Sherrington, Foerster) it seems probable that we are only dealing with a condition in which the threshold of stimulation is extremely low.

Flexor spasms also occur in paraplegia in extension, and in a lesser degree in hemiplegia. In the former case they are usually alternating in time in the two limbs, not simultaneous. In paraplegia in flexion they are often bilateral and synchronous.

The involuntary spasm typical of the extended form of spastic paralysis, however, consists of a sudden increase of extensor tone, usually in both limbs at once, and not producing any actual movement. This jerky spasm is quite unlike the slow powerful flexion reflex, and is allied to the spontaneous limb-clonus so often seen in these cases.

§ 5.—*Reciprocal Innervation in the Flexion Reflex.*

So far I have dealt solely with the muscular contractions in the flexion reflex. Every co-ordinated movement involves, as Sherrington has shown, both excitation and inhibition; excitation and contraction of the "prime movers" (Beever), the flexors in this case, with inhibition and relaxation of their antagonists, the extensors.

Certain muscles are pure flexors, e.g., sartorius; others act as flexors of one joint and extensors of another. Such muscles are the hamstrings, which extend the hip and flex the knee. In the flexion reflex these muscles act as flexors, their extensor action being completely overcome by the hip flexors. Rectus femoris also illustrates this and the further point that muscles which are regarded as units anatomically are not so physiologically; thus, in the flexion reflex, rectus acts as a flexor, while the vasti, being pure extensors, are inhibited. Yet these form part of one muscle—quadriceps extensor femoris. Beever has drawn attention to this separate action of rectus femoris [10].

In the case of pure extensors, such as the vasti, we have clear evidence of their inhibition during the progress of a flexion reflex. The knee-jerk and knee-clonus are evidence of reflex activity in the extensors, and these phenomena are diminished or even abolished by a flexion reflex.

It has long been known that a sudden pinch of the skin of the limb would stop an ankle-clonus, and Brown-Séquard [11] pointed out that clonus ("spinal epilepsy") of a spastic limb could be stopped immediately, and the limb rendered "perfectly supple and pliable" by forcible plantar-flexion of the hallux, but no definite explanation has ever been forthcoming. In the light of the present investigation the cause is clear.

It is found that if the knee-jerk in a case of spastic paralysis be rhythmically elicited and the sole of the limb be then briskly stroked for some seconds, the jerk commonly diminishes in force, even when the reflex flexion is not sufficient to prevent it mechanically.

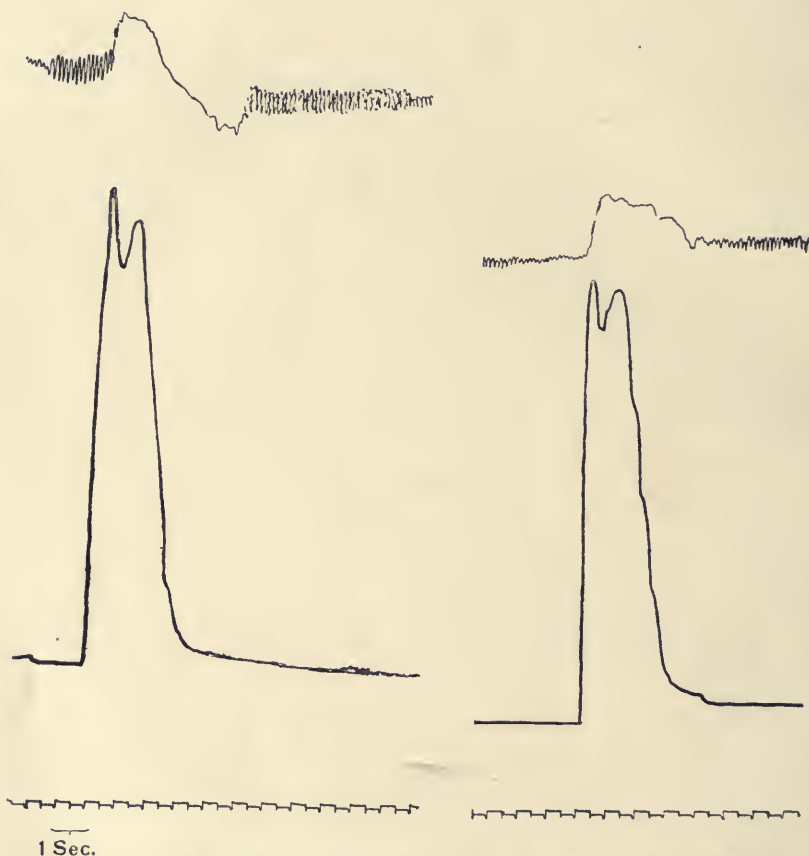


FIG. 5.—The upper tracings record a spontaneous knee-clonus, the lower an “extensor response,” elicited by stroking the sole sharply. There was no power of voluntary flexion of the limb, which was fully extended when recording the reflex movements. While active flexion was in progress the clonus invariably ceased, reappearing at once on the cessation of the flexion reflex. The upward excursion in the upper record was due to some flexion at hip and knee accompanying the “extensor response,” and does not represent any active movement of the patella with which the lever was connected.

The phenomenon can be recorded graphically in the case of a spontaneous knee-clonus which can often be inhibited by light sole stimulation. Fig. 5 is such a record taken from a case of extra-medullary spinal tumour of 7th cervical level, causing spastic paresis

of the lower extremities in extension. The extensor rigidity was intense and spontaneous knee-clonus was frequent. All the tendon-jerks were increased, and the plantar response was "extensor" in type.

Light sole stimulation gave a flexion reflex with very little actual limb flexion, but an ample toe movement. While this lasted the knee-clonus ceased, and recurred when the flexors ceased to be actively contracted; a beautiful example of reciprocal innervation in the flexion reflex.

In fig. 5 note that the upward movement in the clonus curve is due to limb flexion—not to vastus contraction and traction on the patella. This flexion movement could not be abolished completely. The crossed knee-clonus is affected in quite a different manner and will be dealt with in the next section.

We have evidence, therefore, that extensor tonus is inhibited by active contraction of the flexors in the flexion reflex, and we shall discuss, at a later stage, the effect of this constantly maintained extensor tonus on the flexion reflex.

§ 6.—*Reflexes accessory to the Flexion Reflex: Crossed and Homolateral Extension: The Crossed Plantar Reflex.*

Reflexes accessory to the flexion reflex are the crossed extension reflex, the crossed plantar response, and the homolateral reflex extension obtained, in some cases, by stimulation of the skin of the base of the thigh, or of the perineum. This last is independent of the flexion reflex, although it occasionally seems to occur in association with it. Reflex extension is commonly seen, however, in association with reflex flexion as a crossed phenomenon.

Babinski [1], Byrom Bramwell [12], Fairbanks [19] and others have recorded that in certain cases of spastic paralysis in which an "extensor" type of plantar reflex is obtainable, there occurs, on stimulation of the crossed foot, a plantar reflex of "flexor" type. Thus in hemiplegia an "extensor" plantar[?] reflex is obtained from the affected limb, but on eliciting a plantar on the sound side a "flexor" plantar response is seen on the affected side.

Examination of this crossed response shows that it differs fundamentally from the normal plantar reflex, the so-called "flexor response."

In this we see plantarflexion of digits, dorsiflexion of foot, a constant contraction of tensor fasciæ femoris and certain inconstant contractions of the limb musculature.



A



B

FIG. 6.—Homolateral and Crossed Plantar Responses. A, resting position of limbs; B, plantar stimulation of left sole giving flexion reflex (flexion at hip and knee was forcibly prevented by an assistant). On right side a “crossed plantar response.”

The crossed plantar response, examined in the extended limb, consists of plantarflexion of both foot and toes, but no tensor fasciæ femoris contraction.

The contrast is well seen on eliciting a plantar reflex from the normal sole of a hemiplegic in whom the crossed reflex occurs. The dissimilarity between the two is striking.

This crossed reflex would, therefore, seem to be indicative of active extension of the limb, and this is readily capable of proof. If the limb

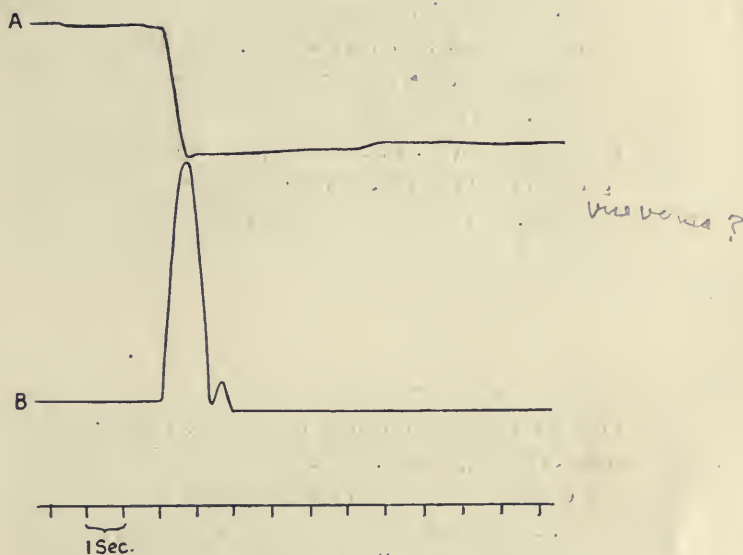


FIG. 7.—Flexion and Crossed Extension Reflexes. A, left limb. This was held supported in flexion by an assistant—one hand under heel, and one over knee to prevent the limb falling laterally; B, right limb. This lay extended and the sole was stimulated by a brisk stroking. Both records are one-eighth of the amplitude of the actual excursion of the limb. Flexion is an upward, extension a downward, movement.

be previously flexed and supported lightly so that no resistance is offered to active extension and the crossed sole then stimulated, there occurs an active extension at hip and knee as well as the movements already described. This is the crossed extension reflex.

The crossed “flexor response” is, therefore, part of a crossed extension reflex. Crossed extension and the crossed plantarflexion, when present, commonly occur together. Rarely the latter is seen alone or without a trace of extension at the hip and knee, and I conclude that, as in the spinal animal, crossed extension may be present only at the distal joints.

Crossed extension at hip and knee without plantarflexion of foot and toes I have not seen.

It is the general rule in cases of spastic paralysis with rigidity in extension and increased knee- and ankle-jerks for the crossed extension reflex to be present, but it is not constantly present. Two photographs and a graphic record (figs. 6 and 7) from a case of spastic paraplegia due to meningo-myelitis show these reflexes.

In this case the legs showed moderate paresis with strong extensor rigidity. All the tendon-jerks were exaggerated, and there was knee- and ankle-clonus, and "extensor responses" from the soles. Crossed extension was constant and very active. When the crossed limb, right or left, lay extended, this was seen as plantarflexion of foot and toes, but when flexed, active extension occurred at all joints.

The photographs (fig. 6, A and B) show the resting attitude of the limbs and the flexion reflex on the stimulated side with the crossed plantar response. The combination of plantarflexion of foot and toe is well seen, and it is obvious that the crossed reflex is not the normal "flexor plantar response."

Fairly strong stimulation of the sole was needed to evoke a good crossed extension and minimal stimuli gave plantarflexion of foot and toe alone, the motor focus evidently being distal in this reflex.

The crossed extension reflex is always, in my experience, a single and not an alternating reflex. There is, it is true, often a flexion rebound after active extension, which is seen as an "extensor response" with slight flexion at all joints. If the whole movement be very rapid, this crossed "extensor response" is apparently synchronous with the homolateral flexion reflex, and I think that the "crossed Babinski" which has been described is of this type, and is not synchronous with flexion in the stimulated limb, but is a rebound following crossed extension, such as Sherrington [36] describes: Figs. 8 and 9 show this photographically and graphically.

The case from which these were obtained was one of acute disseminated sclerosis. When the patient first came under observation the legs showed spastic paresis in extension with a well-marked flexion reflex and crossed extension reflex. The condition in the legs progressed and became that of paraplegia in flexion; as this happened the crossed extension disappeared. (This case is described at length in Appendix, Case 2.)

A well-marked flexion reflex may be present without any evidence of crossed extension, which is no integral part of the reflex. The factor

determining absolutely the occurrence of the crossed extension reflex is the presence of reflex activity in the extensor muscles of the limb. The indications of reflex activity of this group of muscles are increased knee- and ankle-jerks, the presence of clonus and spasticity in extension.



Fig. 8A.



Fig. 8B.

FIG. 8A.—Resting attitude of limbs.

FIG. 8B.—Flexion reflex with "crossed plantar response," consisting of plantarflexion of foot and toes.

These are the conditions found in hemiplegia and in paraplegia in extension, in which alone crossed extension is seen. It is not seen in paraplegia in flexion, which I have found to be characterized



Fig. 8c.

FIG. 8c.—“Rebound” in each limb in opposite sense to original movement.

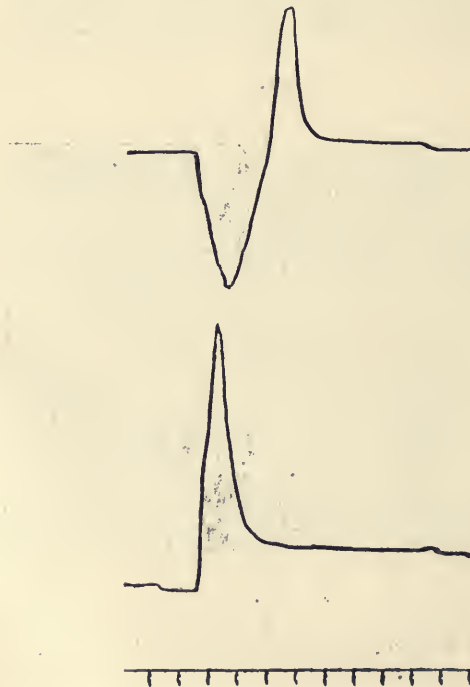


FIG. 9 is a graphic record of the phenomenon shown in fig. 8. The upper tracing shows a crossed plantarflexion followed by an “extensor response”; “rebound” phenomenon. The lower tracing, simultaneously taken, records an “extensor response” elicited from the left sole. The crossed extension is synchronous with this; the crossed “extensor response” is later. This is a direct record of hallux movement. Upward movement indicates dorsiflexion, and downward movement plantarflexion. Time, below, in seconds.

by the absence or diminution of the reflex activity of the limb extensors, while in the flexors this is conserved and increased. The stimulus and receptive field for the crossed extension reflex are those of the homolateral flexion reflex.

In this reflex the muscles which contract are those which in the flexion reflex are inhibited. This increased tone in the extensors I have been able to record graphically, in the case of the knee extensors.

In a case of spastic paraplegia of Erb's type in which there was spontaneous knee-clonus, the eliciting of a plantar reflex, i.e., a flexion reflex, caused an inhibition of the knee-clonus on the same side, but so increased the tonus of the crossed extensors that they went into well-marked tonic spasm, which relaxed and resumed the clonic form on cessation of the stimulus (fig. 10).

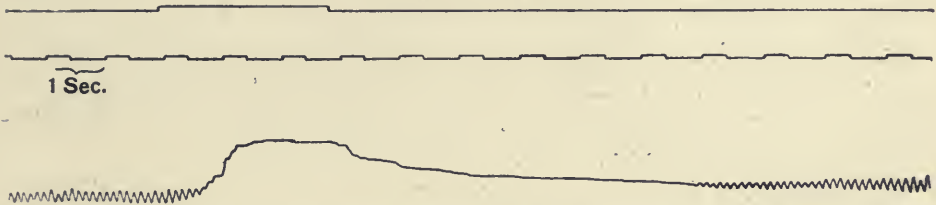


FIG. 10.—Records a spontaneous vastus clonus becoming strong tonic spasm during plantar stimulation of the crossed leg. The upper signal records the duration of the sole stimulus. The lower signal gives time in seconds (two segments to 1 sec.).

In the case from which figs. 8 and 9 were obtained, the same phenomenon was demonstrable in a different way. The condition passed from that of paraplegia in extension to paraplegia in flexion, the right leg being affected earlier than the left. The right knee-jerk failed and soon disappeared. For two weeks after the knee-jerk had ceased to be obtained by ordinary means alone, it could be caused to reappear by simultaneous stimulation of the crossed sole, and for as long as this stimulation lasted. Unfortunately, the jerk thus obtained was too feeble to lend itself to graphic record. But for a period of at least two weeks this reinforcement of the crossed extensors could be seen.

Also, evidence of inhibition of the crossed flexors during a flexion reflex is often obtainable. If, by gentle continued stimulation of one sole, in a case of spastic paraplegia, the hallux be induced to assume an attitude of dorsiflexion, similar stroking of the crossed sole will cause a definite plantarflexion of the toe originally dorsiflexed, in spite of continued stroking of the sole. Of course, increased intensity of the original

stimulus will cause the reappearance of the flexion reflex originally elicited. This brings me to a further fact that the homolateral reflex will, if sufficiently intense, always break through and overcome a crossed reflex of whatever intensity. That is, a relatively weak flexion reflex is more potent than the most intense crossed extension reflex.

The rebound following reflex flexion and crossed extension are also accessory to the flexion reflex, since they follow it. Sherrington [36] has described in all reflex reactions a "post inhibitory exaltation" of activity of the muscles inhibited during the reflex. This certainly occurs in the flexion reflex and crossed extension reflex. In the former as rebound extension, and in the latter as rebound flexion. The latter I have already spoken of, and figs. 8 and 9 illustrate it.

Homolateral extension reflex.—This is of relatively rare occurrence, and I have seen it only five times in the series of cases examined. It is obtained, as mentioned earlier (*see* p. 285), on stimulation of the skin, by pin-prick or pinching, of the upper extremity of the thigh and of the perineum, and consists in a quick extension at hip and knee with plantarflexion of ankle and toes. On the few occasions I have seen it, I have not observed any crossed reflex accompanying it.

Sherrington describes a similar reflex occurring on stimulation of the base of the limb or of the perineum by painful stimuli in animals.

§ 7.—*Factors modifying the Reflexes.*

(a) *Muscle Tone in the limb.*

Thus far, I have described the features of a typical flexion reflex and of a crossed extension reflex. Whenever obtained, the flexion reflex consists of a single movement of flexion of the limb, but it is quite clear that the groundwork of muscle tone into which the reflex breaks must have a modifying effect on it, while in the case of the crossed extension reflex its existence depends on the presence of hypertonus in the extensor group of muscles in the limb.

It is not my intention here to go deeply into the question of contracture and hypertonus, but, regarded broadly, the lower extremity may show either of two conditions in spastic paralysis:—

(1) It may be a limb rigid in extension, with hypertonus pre-dominant in the extensors, which muscles show also, as signs of increased reflex activity, increased knee-jerk and ankle-jerk with clonus. The flexors also show great increase of reflex activity, e.g., the flexion

reflex with the Babinski plantar response, involuntary flexor spasms and increased hamstring-jerks. Such a condition is seen in hemiplegia.

(2) It may be a limb spastic in flexion. In such a case we find evidence that the reflex activity of the extensors is greatly diminished, or absent. The knee-jerks and ankle-jerks are feeble or unobtainable. There is no clonus. The extensors show no hypertonus. The flexors, on the other hand, show extreme reflex irritability. There is a well-marked flexion reflex with its Babinski plantar phenomenon. Involuntary flexor spasms are continual, and reflex flexion is provoked by the slightest cutaneous stimulus to the limb. The hamstring-jerks are very brisk. The muscles do not, it is true, show the steadily maintained hypertonus characteristic of the extensor rigidity, but the limb tends eventually to go into a permanent attitude of flexion. Even then, however, until contracture becomes marked, there are periodical remissions of the flexor spasm, and the legs fall into extension transiently.

In speaking above of the predominance of extensor spasticity, in cases of spastic paralysis in extension, I do not necessarily imply that when a lesion gives rise to such a condition the extensors are *more* affected than the flexors. I would rather suggest that they are *differently* affected, and that while the extensors show their separation from a higher centre, or their liberation from cortical control by entering in a condition of maintained hypertonus, which might, using Sherrington's phraseology, be called a "static reflex," the flexors indicate their liberation characteristically, in the appearance of the flexion reflex—a "phasic reflex." Both muscle groups show increased tendon-jerks.

Whether this view be accepted or not, it is certain that the leg, in cases of spastic paralysis, must conform to one or other type, except in conditions of "spinal shock," when the extensors show no sign of reflex activity and that of the flexors, though present, is minimal. These special conditions will be discussed later.

We are able then, except in this third case, to examine the flexion reflex under these two conditions; with and without the presence of extensor reflex activity in the limb.

These two types of paraplegia, the clinical characteristics of which have been emphasized by Babinski [2, 5], and named by him "paraplegia in extension," and "paraplegia in flexion," give us the opportunity of examining the effect which a groundwork of hypertonus in the extensors has on the flexion reflex. This reflex employs the flexors, while the antagonists of these muscles, the extensors, are by reciprocal innervation inhibited during the progress of the reflex.

The flexion reflex in paraplegia in extension.—In this type of spastic paralysis the flexion reflex is characterized by being less easily elicited in the ample form seen in paraplegia in flexion. The toe movement may be the only actual movement visible, though palpation of the hamstrings will reveal invariably a contraction of these muscles.

The reflex movement is, when it involves actual flexion at hip and knee, always rapid, and is followed immediately on cessation of the exciting stimulus by quick active extension "rebound." It is in these circumstances that intermittent flexion is found. Fig. 11 records this unequally maintained flexion. In this there is no true alternating flexion and extension. The condition is one in which a flexion reflex incompletely overcomes a strongly maintained hypertonus in the antagonists; a static reflex is broken into imperfectly by a phasic reflex.

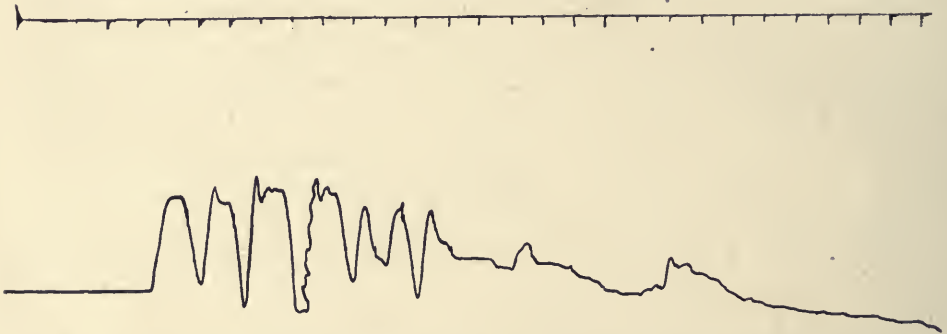


FIG. 11.—Intermittent flexion reflex obtained by continued pinching of the skin of the thigh. The stimulus is not recorded, but it did not cease until reflex movement had already died away. Signal records time in seconds.

The case from which this record was obtained was one of cerebro-spinal lues, with spasticity of the legs in extension. In these circumstances the flexion reflex consisted of an excitation of the flexors, which broke into a maintained hypertonus of the extensors. This it temporarily and imperfectly inhibited and replaced.

Dependent also on this extensor tonus is the crossed extension reflex, which never occurs except when the extensors show increased reflex activity. In cases of increasing paraplegia in which the legs go into an attitude of flexion, this crossed reflex disappears *pari passu* with the diminution of extensor hypertonus, knee-jerk and ankle-jerk.

The crossed extension reflex is only seen therefore, clinically, in cases of hemiplegia and of paraplegia in extension. It does not occur in paraplegia in flexion (*see Case 2, in Appendix*).

The flexion reflex in hemiplegia is very like that obtaining in paraplegia in extension as regards extensor rebound and the presence of the accessory crossed extension reflex. In hemiplegia, however, the severance of the lower motor centres from voluntary control is less complete than in most cases of paraplegia, so that the flexion reflex tends to be more facile in the latter. There are other modifications, too. The receptive field is often confined to the foot, sole and dorsum, for cutaneous stimuli, and to below the knee for deep muscular stimuli (Oppenheim's procedure). The response is seldom ample, but is true to type in that the "Babinski response" is accompanied by palpable hamstring contraction. The reflex, in other words, though present and complete in form, is less facile and less ample; less uncontrolled.

Crossed extension is present, and can be elicited by stimulation of the sole on the normal side.

In paraplegia in flexion.—In these cases the flexion reflex reaches its greatest development, and in the transition from paraplegia in extension to this condition the involuntary flexor spasms increase in power and frequency, until an attitude of flexion is attained. Even in this the phasic character of the reflex is seen in transient intermissions, partial or complete, of the flexor "spasticity."

The receptive field is very wide and may reach the abdominal wall for pin-prick. Light stimuli suffice, and the minimal reflex responses are complete, ample and strong.

In these cases the "extensor response" is to the most superficial observation, not an isolated phenomenon, however lightly obtained. The muscles activated are the flexors only and the response never involves the extensors of the limb. There is usually no active rebound, but the momentary diminution of tone that follows a reflex may allow the limb to extend passively with gravity. There is no crossed extension reflex with its plantarflexion of foot and toes.

In cases of extreme spasticity in flexion, we occasionally see a crossed flexion reflex, synchronous with—or slightly later than—the homolateral flexion reflex. There is no doubt that, in cases with diminished or absent extensor reflex activity and increased flexor reflex irritability, a crossed symmetrical reflex flexion may occur. It is, however, exceptional, though it accounts for a small percentage of cases of so-called crossed "extensor response."

Intermediate between the two groups of spastic paralysis is a class of progressive spastic paraplegias, from compression or intramedullary lesions of various kinds, in which we are able to see a transition from paraplegia in extension to paraplegia in flexion.

This change is only found in increasingly extensive transverse lesions, i.e., it depends on more and more complete severance of cord and brain. It is characterized, as I have already pointed out, by *progressive disappearance of reflex activity in the extensor group of muscles*. As this change goes on, the flexion reflex tends to become more facile and forcible. It no longer has to overcome a maintained reflex tonus in its antagonists.

A final condition is that of "spinal shock." This is seen in cases of complete transverse lesion of the cord, and in coma preceding death. Case 1 in Appendix is an example of the former.

Lewandowsky and Neuhof [27], and Dejerine and Valensi [16], have reported cases of complete cord lesion, verified by autopsy, in which signs of reflex activity were present in the legs.

In Lewandowsky's case, an "extensor response" was obtained, and also "reflex contractions of the thigh muscles." Following prolonged faradism an ankle-jerk was also transiently obtained.

In Dejerine and Valensi's case, pinching of the skin of the thigh gave a brisk flexion at hip and knee, but for mechanical reasons no "extensor response." In both cases there was complete flaccid palsy with sensory loss and absent tendon-jerks.

In three cases of my series there have been, according to Bastian's [9] law, complete transverse lesions. One case is given at length (Case 1, Appendix). All showed the presence of reflex activity in the flexors, and in these muscles alone. This was, it is true, minimal, and reflex flexion could only be obtained from the distal extremity of the limb. In each case the minimal response was a hamstring contraction. In one case, at onset, no toe movement was obtained, only flexion at hip and knee. All were characterized, as were the cases quoted above, by complete absence of any signs of reflex activity in the extensors. This fact is most significant. In the higher animals, e.g., monkey, recovery from "spinal shock" is late and very incomplete, occurring much later and less completely in extensors than in flexors. In man, shock is more profound, but, for a period at least, there is evidence of reflex activity in one group of muscles, the flexors, until "isolation dystrophy" destroys all possibility of spinal cord function.

(b) *Sensory Disturbances in the Limb.*

The interruption of central afferent paths has no effect on the flexion reflex. As typical a flexion reflex is seen in cases with complete as in those with no sensory loss.

In a case of lesion of the lower dorsal cord of sudden onset following parturition, and probably thrombotic in origin, there was complete motor paralysis and sensory loss in the lower limbs. Bedsores rapidly developed and very shortly the legs went into flexion, and the typical clinical picture of paraplegia in flexion, as described by Babinski, resulted. There was a very facile and powerful flexion reflex and "extensor plantar response." Within two months the sensory disturbance cleared up entirely and at present sensation is normal. The motor paralysis and attitude of flexion of the limbs remain almost unchanged, as does also the flexion reflex. It is in cases of paraplegia in flexion that the flexion reflex is best developed. Such cases are generally indicative of severe involvement of the cord, either by compression or in advanced intramedullary lesions, e.g., transverse myelitis, disseminated sclerosis. Very commonly profound sensory loss is present and it is in these cases that we see the reflex movements to best advantage, since all voluntary effort and control are absent, and the patient is unaware both of stimulus and response.

It may be said, therefore, that even profound interruption of central afferent paths has no modifying effect on the flexion reflex.

As regards the crossed extension reflex, it is not possible to make so absolute a statement. As already pointed out, this reflex depends for its occurrence on the presence of a reflexly active extensor group of muscles. Now, in cases of complete or extreme sensory loss, it is not the rule to find this condition, rather do we find the more advanced condition of paraplegia in flexion in which no crossed extension reflex occurs. I conclude that the integrity of at least some afferent paths to the brain is essential for the presence of reflex activity of the extensors.

Any interruption, however, of the afferent side of the spinal reflex arc at the appropriate level, if sufficiently complete, will cause the disappearance of all reflex activity.

CHAPTER IV.—SUMMARY OF CLINICAL FINDINGS.

(1) In spastic paralysis of the lower limbs the most common reflex movement is that of flexion. This consists, when complete, of flexion at the hip and knee with dorsiflexion of the foot and toes, more especially of the hallux. I speak of this as the flexion reflex of the lower limb. It occurs as the apparently spontaneous flexor spasms so prominent in many cases of spastic paraplegia, and on appropriate stimulation of the limb.

(2) The reflexogenous area or "receptive field" of the reflex comprises the skin and deep structures of almost the entire limb. The threshold of stimulation is lowest on the sole, especially over the outer half.

In general, stimuli of "nocuous" or harmful character are most adequate to produce a reflex, but, on the sole, light painless pressure applied by stroking will evoke a reflex response.

From the proximal fourth of the thigh, reflex extension is sometimes obtained. This is infrequent, and apart from the crossed extension accessory to the flexion reflex, reflex movements of extension hardly ever occur.

(3) The "extensor" type of plantar response never occurs without evidence of reflex contraction of more proximally situated flexor muscles, notably the hamstrings. And conversely, a flexion reflex always includes the dorsiflexion of the hallux, known as the "extensor response." Both are elicited in the same manner and from the same receptive field. They are inseparable and are clearly parts of the same phenomenon.

(4) Inhibition of the extensors of the limb—the antagonists of the contracting muscles—is seen in the flexion reflex as inhibition of the knee-jerk and knee-clonus, and as diminution of the hypertonus of the extensors while active flexion lasts; following this, "extensor rebound" may be seen.

(5) When the limbs are spastic in extension, a crossed extension reflex may occur on eliciting a flexion reflex. Of this crossed extension reflex, plantarflexion of the foot and toes is a part, and constitutes the "crossed plantar reflex" of Babinski and others. Both flexion and crossed extension reflexes consist in a single movement of the limb of the same duration as the exciting stimulus, and showing no rhythmic character.

(6) The occurrence of a crossed extension reflex depends on the existence of a high degree of reflex activity in the extensors, such as is found in the affected limb in hemiplegia and in "paraplegia in extension." It never occurs apart from this.

(7) The flexion reflex is seen at its highest development in the condition of "paraplegia in flexion," in which, the limb extensors having lost their reflex activity, that of the flexors, which is phasic in type, has reached this extreme form, where it constitutes the condition in question.

(8) The two clinical forms of spastic paralysis of the legs, first clearly described by Babinski, are found to have this essential difference: that

while the extended form shows reflex activity in both flexor and extensor groups of muscles, the flexors alone retain this in the flexed form. In paraplegia in flexion the knee- and ankle-jerks may be absent, but the hamstring-jerks are always brisk. The statement, therefore, that the tendon-jerks may be absent in this type of spastic paralysis is not correct. They still exist in the only muscles with reflex action, namely, the flexors.

(9) Comparison of the two forms shows that the specific reflex action of the extensors consists in the maintenance of a high degree of tone in these muscles, "*a static reflex.*" The flexors, on the other hand, under the same conditions of pyramidal tract affection, develop *a reflex activity "phasic" in type*, giving rise to reflex movement.

CHAPTER V.—PHYSIOLOGICAL CONSIDERATIONS.

§ 1.—*The Physiological Significance of the Flexion Reflex and of the "Extensor Response."*

It is abundantly clear that the reflex phenomena occurring in the lower limbs, as an accompaniment of pyramidal tract affection, present the closest possible analogies with those described by Sherrington in his animal experiments. We must now consider whether they are capable of the same explanation, and whether we are justified in applying to man the conclusions at which Sherrington has arrived as the result of his physiological researches on animals.

The flexion reflex, including the dorsiflexion of the foot and hallux, which has been shown to occur in man, on the application of appropriate stimuli to the limb, and the crossed extension reflex which may accompany it, are strictly analogous with the flexion and crossed extension reflexes of the hind limb of the spinal and decerebrate animals, in regard to the nature of the stimulus, the extent of receptive field and the form of the motor response, in each instance.

Sherrington concludes that this reflex is protective in function. It differs from "spinal stepping" in that it is a single and not an alternating reflex, and that it is elicited by a totally different form of stimulus. Nocuous stimuli applied to the limb produce a single flexion, i.e., a flexion lasting with the stimulus, and never an alternating flexion and extension. "Spinal stepping," on the other hand, is characteristically alternating and rhythmic, and is elicited by passive movement of the limb—never by cutaneous nocuous stimuli applied to it.

Is the reflex obtained clinically in man, then, of the nature of a

protective reflex, Babinski's "Réflexe de défense," or does it partake of the nature of "spinal stepping"?

Marie and Foix [30, 31] are of opinion that the reflex is analogous with "spinal stepping," and has no protective significance. They point out that the movement obtaining in it is unvarying in form, whatever the site of the stimulus, and shows no trace of adaptation to circumstances. For, although the movement is one of withdrawal when the sole is stimulated, the same movement in response to stimulation of the thigh constitutes an actual approach to the site of injury. The reflex cannot, therefore, they say, be protective.

However, the fact cannot be overlooked that when the reflex activity of the limb is at its lowest, as in "spinal shock," and when the causative lesion is confined to the pyramidal tract, as in hemiplegia, the receptive field of the reflex is minimal, and in these circumstances is limited to the sole, or even to a part of the sole. Further, the threshold of stimulation is always lowest on the sole, and no matter what the extent of the receptive field, a response is always to be obtained here. The sole is, therefore, the most essential part of the receptive field; and a reflex, with the characteristics I have described, elicited most readily from the sole by stimuli of nocuous character, may surely be regarded, legitimately, as protective in function.

A more important objection to the opinion held by these authors, however, is that it does not seem to recognize the essential differences between the nociceptive flexion reflex of Sherrington and "spinal stepping," differences which completely distinguish the two reflexes and prove the identity of the one we are considering with the flexion reflex of the hind limb of the spinal animal. The alternating and rhythmic movement of the locomotive reflex of the spinal animal is obtainable by passive extension of the flexed limb; i.e., by proprioceptive stimuli, or by nocuous cutaneous stimuli applied to the opposite limb or the skin of the perineum, i.e., remote from the reacting limb, while the single movement of the flexion reflex is elicited by nocuous stimulation of the reacting limb, and never by crossed or proprioceptive stimuli.

As to the relationship between the flexion of the limb and the "extensor plantar response," various views are held by different authors. Marie and Foix [31] and Noica [33] believe that the two phenomena are part of a general flexion of the limb. According to these authors the "extensor response" is the minimal manifestation of a reflex automatic movement of general flexion, which itself is but a part of the complex motor mechanism of progression. That it is part of the flexion reflex

my observations have clearly shown, but analysis of the reflex in varying conditions of development has demonstrated, in addition, that it is not the minimal motor response, this being found in the inner hamstrings, as Sherrington has also found to be the case in the flexion reflex of the spinal animal. Marie and Foix have recorded a further interesting point, which I am able to confirm, that when the reflex is elicited by stimulation of the proximal part of the receptive field, the "extensor response" is less ample and may even fail. This is the phenomenon referred to by Sherrington as "local sign," and which I have mentioned already.

Babinski, by whom the "extensor response" was first described under the name of "le phénomène des orteils," while regarding the limb flexion as defensive in nature, considers the "extensor response" to be a distinct and separate reflex, a thing apart, for which he offers no explanation, and which remains for him a mystic and inexplicable sign of pyramidal tract affection.

In support of his view he instances cases in which reflex flexion of the limb was accompanied by plantarflexion of the hallux, i.e., by a "flexor response." But I have shown, and figs. 3 and 4 record, that where actual plantarflexion does accompany flexion at hip and knee, the two phenomena are not synchronous, and that a dorsiflexion of foot and hallux, that is, an "extensor response," does occur as part of the reflex flexion.

Babinski also refers to a case recorded by Dejerine and Valensi [16], and verified at autopsy by Dejerine and Long [17], in which, following total transverse lesion of the cord, there was a strong reflex flexion to be obtained on pinching the skin of the thigh. On stimulating the sole, however, a plantarflexion of the hallux resulted. From this, both Babinski and Dejerine conclude that the two phenomena are separate and distinct.

Reference to the original clinical description of the case in the *Revue Neurologique* reveals the following statement: "Les pieds sont en varus-équien et les orteils en flexion. Cette déformation est aujourd'hui fixée par des rétractions fibro-musculaires. . . . Le réflexe cutané plantaire se fait en flexion et il est plus fort à droite." It is difficult to see how any other movement than plantarflexion could occur in the circumstances, and the observation and inference are alike valueless.

Finally Babinski [6] has shown that the application of an Esmarch's bandage to the spastic limb causes a transient conversion of the "extensor response" to a plantar response of normal "flexor"

type, which at once gives place to complete absence of plantar reflex, although at the same time the defence reflexes are greatly increased in intensity. Since the two phenomena are so differently affected by this procedure, he infers that they must be separable and distinct.

It can be demonstrated, however, as Marie and Foix have shown, that this experiment is quite illusory. The application of the bandage is such as to render ischæmic the muscles involved in the "extensor response," but not those causing flexion at hip and knee, while at the same time it acts as a strong stimulus to reflex flexion, in which, naturally, the ischæmic muscles take no part. On the first application of the bandage, the "extensor response" becomes "flexor" in type and then all plantar response disappears. This transient conversion, Marie and Foix suggest, is due to the fact that the more superficial anterior tibial group of muscles, subserving the "extensor response," are rendered bloodless earlier than the deep plantar muscles responsible for the plantarflexion.

There is nothing, therefore, in these arguments brought forward by Babinski to invalidate the view held here as to the nature of the "extensor response," which my observations show to be part of the flexion reflex of the limb. It is always present in the fully developed reflex, and conversely, when it occurs it is invariably accompanied by reflex contraction of the proximal flexors of the leg, notably of the inner hamstrings, which are the motor focus of the reflex.

Van Woerkom [43] is another author for whom the "extensor plantar response" is a reflex in itself. To account for it, he advances a hypothesis, which may be briefly described as based on the supposition that primitively the hallux is a prehensile organ with movements peculiar to itself, to which it reverts in condition of pyramidal tract involvement. This view is interesting, but must remain purely speculative, and is certainly superfluous.

I conclude, therefore, not only that the flexion reflex of the lower limb, obtained as here described, is a reflex, protective in function and strictly analogous with the nociceptive flexion reflex of the hind limb of the spinal (or decerebrate) animal, but also that the "extensor response" is an integral part of this reflex.

The "extensor response" becomes, according to this hypothesis, part of a co-ordinated, purposive movement complex, and it is interesting to consider how it compares in this respect with the normal type of plantar reflex—the "flexor response."

The relationship of the two phenomena has been the subject of much

discussion. Babinski, in dealing with the "skin reflexes," observes that whereas the abdominal reflexes disappear in pyramidal lesions, the plantar reflex, which is regarded as belonging to the same class of reflex, undergoes a qualitative change. V. Gehuchten [41] divides skin reflexes into normal and pathological. The former disappear in lesions of the pyramidal tract, the latter only appear in these circumstances. He supposes, then, that the normal plantar reflex has gone, and has been replaced by a new reflex.

According to Marie and Foix, and in this respect my observations would tend to confirm their view, the normal plantar response is a unisegmental reflex strictly comparable with the abdominal and cremasteric reflexes, and involving no co-ordination whatever, that is, no reciprocal innervation; it disappears in pyramidal lesions, being replaced by a new reflex, which is not purely cutaneous, and which is a co-ordinated movement, namely, the flexion reflex. In the normal plantar reflex we see on stimulation of the first sacral segmental skin area, a simple contraction of muscles innervated from this segment: the short flexors of the digits and tensor fasciæ femoris.

I have described the variability of the contractions of the adventitious muscles in the "flexor response," and the participation in the movement of muscles belonging to both flexor and extensor groups. I would further draw attention to the extremely limited receptive field of the normal reflex and to the fact that it is indeed a cutaneous reflex pure and simple. It differs fundamentally, therefore, from the pathological plantar response.

In addition to the flexion reflex, I have described a crossed extension reflex, and I have shown that the crossed plantar reflex bears the same relation to this that the "extensor response" bears to the flexion reflex; namely, that the foot and toe movement in each case does not constitute the whole reflex movement, but merely the most readily apparent part. In the case of the crossed extension reflex, therefore, the full extent of the movement is only seen if the reacting limb is held passively flexed while stimulating the crossed sole. If this be not done, a plantarflexion of the foot and toes is the only visible response.

Contrary to what has been assumed, this crossed plantar reflex differs from the normal "flexor response"; and I have described how this difference in form may best be seen.

Complete analysis of the crossed extension reflex shows that it bears the closest possible analogy with the crossed extension reflex of Sherrington's animals, in regard to the character of the exciting

stimulus and the extent of the receptive field, the form of the response, and the circumstances under which it occurs. Obtained as a reflex accessory to the flexion reflex it has this further interest, that it affords convincing evidence that the processes of reflex action and motor innervation in man show no essential or qualitative differences from these physiological processes in animals, and I propose to develop this analogy still further in the succeeding section.

In the meantime, a reference is necessary to the occasional occurrence of a "crossed extensor response," i.e., a "Babinski response" obtained on stimulation of the opposite sole.¹ This is only seen under certain specific conditions, in my experience. In the extended form of spastic paralysis of the lower limb, homolateral flexion is always accompanied by crossed extension, when any crossed reflex is seen, and this connotes crossed plantarflexion of foot and toes.

However, where the reflex activity of the extensors is relatively less than that of the flexors—namely, in paraplegia in flexion, and in conditions transitional between this and the extended form of spastic paralysis—we do see a crossed flexion reflex with its integral "extensor response." In such cases occur bilateral spontaneous flexor spasms. Sherrington has noted, in certain parallel circumstances, the occurrence of crossed reflex flexion. In man, therefore, as in animals, there is this occasional exception to a general rule laid down by Sherrington, that in the hind limbs of the spinal animal simultaneous reflex movements are opposite in phase in the two limbs.

The phenomenon of "flexor rebound" following crossed extension is, however, as I have shown (*see* figs. 8 and 9) responsible for a certain proportion of "crossed extensor responses."

¹ In view of the fact that the "extensor response" is part of a general movement of flexion, while the toe movement in the normal plantar response, the "flexor response," is, physiologically considered, a movement of extension, it is unfortunate that the accepted terminology is the direct converse of the facts. The expressions "extensor response" and "flexor response" are widely used by neurologists in this country, and I have therefore been compelled to make use of them, though it is very difficult to prevent confusion in the mind of the reader when speaking of a "crossed extension reflex" and of a "crossed extensor response"; two very different phenomena involving antagonistic groups of muscles.

I wish, therefore, to emphasize that these empirical and misleading names are used here in their accepted sense, and have no physiological connotation such as the terms "flexion reflex" and "crossed extension reflex" have. I have consequently placed them in inverted commas to avoid as far as possible all confusion.

In spite of the obvious objections arising from the practice of applying the name of the discoverer to any clinical phenomenon—and the literature on the subject of the reflexes provides many striking examples of this abuse—it seems almost better to speak of the "Babinski response" or of "Babinski's toe phenomenon" rather than to employ terms having a false physiological significance. This is more especially so in this instance, in view of the inevitable confusion that must follow any attempt to correct the present terminology.

§ 2.—*The Dual Nature of the Motor Innervation of the Limb.*

My observations have further established a point of great significance in the study of spastic paralysis, and one not hitherto appreciated; namely, the relationship between the two clinical forms of this condition, in the lower limbs.

It is not my purpose in this paper to deal extensively with the question of contracture except in so far as it concerns the reflex movements of the limb. The two phenomena are intimately connected, as I have already shown in the case of paraplegia in flexion, a condition in which the extensor muscles show diminished or absent reflex activity, while their antagonists, the flexors, show a high degree of reflex activity.

The complete differentiation of the reflex action of the musculature into two systems by the processes of disease, as seen in this form of spastic paralysis of the lower limbs, affords a striking proof of the existence of two systems of motor innervation in man, which are strictly comparable with those differentiated in animals in Sherrington's researches.

I have, in an earlier part of this paper, briefly alluded to this double motor innervation of the musculature of the limb in animals, and a more detailed reference is necessary.

Sherrington has shown that in the innervation of the musculature there are two great reflex systems, each employing in a characteristic manner its own group of muscles.

One system uses the extensor muscles and maintains in them a steady tonus which enables the decerebrate animal to stand, and which Sherrington [38] regards as an expression of reflex posture. The central nervous mechanism of this reflex must be situated in the brain-stem, since it is found only in the decerebrate animal. After transection of the cord at, or below, the caudal end of the pons, the reflex tone of the extensors—the “decerebrate rigidity”—disappears, and a condition of “spinal shock” ensues. This affects only the previously tonic muscles, the extensors, the flexors showing a slight and transient depression.

The other reflex system employs the flexor muscles of the limbs, and its reactions are characteristically phasic, that is, they consist of reflex movements. This reflex is purely spinal, since it is unaffected by severance of cord from brain. Certain of the reactions of this system are protective in function, for example, the flexion reflex of the hind limb. Reflexes of this type are characteristically elicited by nocuous stimuli; they are the least affected by “spinal shock” of all reflex

reactions, and emerge earliest from it. They are "prepotent"; that is, they can replace reflexes of other forms, and most easily the tonic postural reflex of their antagonists, the extensors.

In the decerebrate animal both these reflex systems are found in a state of uncontrolled activity. The limb extensors show a maintained tonus—a static reflex; while, by appropriate stimulation of the limb, reflex movements of the flexors can also be obtained, which break through and temporarily replace the tonic postural reflex. While active flexion is in progress the extensors are inhibited, but resume activity with a momentary increase when flexion ceases. This "post-inhibitory exaltation" of activity is known as "extensor rebound."

The question of the actual identity of the "prespinal centre" for the extensor reflex mechanism will at once be raised. It must be admitted that the evidence of its existence is purely physiological. Yet if this be sufficiently great, we are justified in speaking of such a centre, although its morphological identity may be uncertain.

The physiological proofs can be summarized as follows: An animal whose brain-stem has been transected at the level of the anterior corpora quadrigemina, exhibits a state of active muscle-tone in a physiological muscle group, and in this group alone. Section of the afferent nerve of a muscle in this group abolishes its tone. The reflex arises, therefore, in the muscle itself. Section of the posterior columns of the cord does not abolish the reflex, but section of one lateral column abolishes it below the level of section. The central paths of the reflex arc, therefore, appear to lie in the lateral columns. More precise details of their identity are wanting. A second transection of the central nervous system, at any level below the caudal end of the pons, completely abolishes the reflex below this level. The grey matter, then, of this reflex arc lies at a "prespinal" level. Thiele [40] has shown that the actual level is that of the plane of the paracerebellar nuclei, and with Horsley and Clarke [14] has demonstrated these nuclei to be the source of the "decerebrate rigidity" of Sherrington, that is, of the "cerebellar influx" of Jackson. Sherrington also finds that ablation of the cerebellum itself does not abolish the rigidity [36].

There is, therefore, clear evidence of the existence of a reflex centre placed within a certain area of the brain-stem, limited anteriorly by the anterior limits of the mid-brain, and posteriorly by the level of the plane of the hinder end of the pons. It is not in the cerebellum.

As yet this has not been finally identified with any specific mass of grey matter in the brain-stem. Nevertheless, there is adequate

evidence of the existence of this centre governing extensor tonus in the limb musculature, and probably situated in the paracerebellar nuclei.

The identity of the efferent path from this reflex centre, Sherrington does not specify further than to say it is in the lateral column, *but it cannot be the pyramidal tract, since this has already been interrupted by the decerebration. It must, therefore, be an extrapyramidal motor path.* The significance of this will be seen later.

In the purely spinal animal, the reflex activity of the flexor muscles is as great as in the decerebrate, indeed the threshold of stimulation of the flexion reflex is even lower. Such activity as the extensors now show is secondary to flexor reflexes, and only occurs in protective reflexes or in spinal stepping, as a phase in an alternating movement of the limb. The flexors, therefore, have their centre in the spinal grey matter. In each case the integrity of an afferent path from the muscle to the reflex centre is essential, and section of this, or "de-afferentation" of the muscle, abolishes all reflex activity in that muscle.

Sherrington [36] sums up the matter as follows: "Two separable systems of motor innervation appear thus controlling two sets of musculature; one system exhibits those transient phases of heightened reaction which constitute reflex movements; the other maintains that steady tonic response which supplies the muscular tension necessary to *attitude*. . . . These two systems, the tonic and the phasic reflex systems, co-operate, exerting influences complementary to each other upon various units of the musculature."

To what extent are we justified in applying these conclusions to the elucidation of the phenomenon of spastic paralysis in man?

Clinically, we are not concerned with actual decerebration, but in hemiplegia we have a condition amounting to unilateral decerebration as far as the motor innervation of the limb is concerned.

In hemiplegia the function of the great corticospinal motor path is partly, or completely, abrogated and on analysis we find that the condition resulting in the lower limb presents the closest possible analogies with that of the hind limb of the decerebrate animal.

In hemiplegia, and in any spastic paralysis due to a lesion confined to the pyramidal system, we find a spastic paralysis of the limb varying in intensity, but absolutely constant in type.

In a typical hemiplegia, or lateral sclerosis of the cord, the lower limb lies fully extended with the foot plantarflexed. The limb extensors are very rigid and present brisk tendon-jerks, namely knee-jerk, ankle-jerk, and possibly clonus. This group of muscles also retains relatively

more voluntary power than its antagonists, the flexors, which muscles show less of the spasticity characteristic of the extensors; for example, passive flexion of such a limb often requires considerable force, but once flexed there is no muscular resistance to passive extension.

Wernicke and Mann [29] first recorded both this selective distribution and inverse relationship of weakness and spasticity.

In addition to the spasticity of the limb we note in the flexor group of muscles a brisk tendon-jerk in semimembranosus and semitendinosus, and the presence of reflex movements of flexion with the "extensor response."

That is, both extensor and flexor groups of muscles show a condition of increased and involuntary reflex activity, manifested as hypertonus in the extensors and as reflex movement in the flexors.

This clinical picture, which Babinski [2] calls that of spastic paralysis "en extension," and German authors, "Streckkontraktur," is characteristic of a cerebral lesion, or of any lesion, spinal or cerebral, limited to the pyramidal tract. As regards spinal lesions, Babinski [2] considers that it is in systematic lesions of the pyramidal tract in the cord that the condition characteristically occurs, while Oppenheim notes the extreme rarity of flexion contracture of the legs in amyotrophic lateral sclerosis and other pure pyramidal tract lesions, and says that it only occurs as a terminal phenomenon.

All authors are agreed that in hemiplegia the extensor form of spasticity is constant. The fact is so significant that I think it cannot be too well emphasized. Lewandowsky [26] speaking of hemiplegia says, "im allgemeinen die typischen Verteilung der Kontraktur auf die Beuger am Arm und die Strecker am Bein zustande kommt." Oppenheim [34] is equally explicit: he says, "Beugekontraktur des Beines kommt nur selten und wohl nur unter ungewöhnlichen Bedingungen vor." V. Monakow [32] also emphasizes this point: he says, "Flexionskontraktur (Verkürzungskontraktur) der unteren Extremitäten cerebralen Ursprungs (nach Hemiplegie und als Spätkontraktur) ist sehr selten; sie kommt nur dann vor, wenn ernstliche nutritive, die passive Verkürzung fordernde Störungen in der Muskeln selbst vorhanden sind, oder wenn zu der gewöhnlichen hemiplegischen Kontraktur noch protrahierte Muskelkrämpfe (corticale event. mesencephalen Ursprungs) hinzutreten."

The cases recorded of flexion contracture of the leg in hemiplegia are exceedingly rare. Devic and Gallavardin [18] have described such an instance, in which the lesion was a hæmorrhage in the internal

capsule. The affected leg was the seat of strong flexor spasms which, from the description given, appear similar to those familiar in paraplegia in flexion. The state of the deep reflexes in the limb is not stated, and it is not possible to say whether the two conditions are really comparable.

In the patients I have examined in the National Hospital and in a large series of old-standing hemiplegias which I have had the opportunity of seeing in the St. Marylebone Infirmary, I have not met with flexion contracture in the leg. Nor have I ever seen it in spinal cord lesions, where involvement of structures other than the pyramidal tract could be excluded. In amyotrophic lateral sclerosis, paraplegia in extension is the rule, and only very rarely in the terminal stages of the condition does flexion contracture occur. The *degree* of pyramidal involvement has no influence on the *form* of spasticity in the leg, and *we may conclude, therefore, that a pyramidal lesion, when uncomplicated, gives rise always to the extended form of spastic paralysis in the lower limb.*

Horsley [24] has pointed out the identity of the "decerebrate rigidity" of animals with the rigidity of the leg in hemiplegia, and if in the latter condition we analyse the state of the two muscle groups in the lower limb, the extensors and the flexors, we find the most striking resemblance to "decerebrate rigidity." In both instances we see an extensor group of muscles showing a maintained hypertonus—a "static reflex," and a flexor group showing, as its characteristic form of activity, movement—a "phasic reflex," but not rigidity such as is found in the extensors.

In connexion with this question of a specific type of reflex activity in each of the two muscle-groups, it is not, of course, suggested that the extensors show no phasic activity, or that their antagonists the flexors, have no residual tonus. The presence of alternating movements of the limbs, involving reflex extension as a phase, negatives such a suggestion. Also, the presence of brisk hamstring-jerks, in all cases of spastic paralysis, indicates that the reflex activity of the flexors is not absolutely phasic, but rather shows, to use Sherrington's phrase, "phases of heightened activity." It is clear, however, that in spastic conditions of the lower limbs, the activity characteristic of the extensor muscles is in the form of "tonus," while that of the flexors is phasic, and consists of movement.

We know from the work of Sherrington that decerebrate rigidity is a reflex phenomenon depending on the integrity of a reflex arc passing

from muscle to reflex centre in the brain-stem and thence to the muscle again. We also know that the afferent and efferent links in the arc lie in the lateral columns of the cord. I have pointed out that, since decerebration has interrupted the pyramidal tract, the efferent path for the tonic impulses evoking the characteristic rigidity in the extensors must be an extra-pyramidal one.

Spinal transection severs this path, with the result that the extensors lose their tone, and henceforth show practically no trace of reflex activity. The flexors, on the other hand, which have never been the seat of maintained hypertonus, continue to show unimpaired reflex activity of the specific phasic type. It is thus evident that the efferent path conveying tonic impulses to the extensors has no physiological connexion with the flexors, the reflex action of which is, therefore, seen to be purely spinal.

It becomes of interest to see whether in man, in the parallel condition of spastic paralysis in extension, we have any evidence of the existence of a special extrapyramidal motor path determining in the extensors of the leg the tonic rigidity which is seen to occur, and which, as has been pointed out, so closely resembles the decerebrate rigidity of animals. If this be so, it should be possible to recognize a type of spastic paralysis analogous with the condition found in the spinal animal, in which the flexors alone retain reflex action. Such a phenomenon would be evidence of the existence of a motor innervation of the extensors, other than that depending on the integrity of the pyramidal tract.

In certain severe spinal lesions we do, as I have shown, actually find a type of spastic paralysis, which on analysis is seen to reproduce minutely the state of affairs found in the spinal animal.

This is the condition described by Babinski as paraplegia in flexion. Babinski has found that this clinical type of spastic paralysis occurs commonly in severe diffuse spinal lesions. That it is never seen in cerebral lesions, I have already observed. It is well known, and my observations have confirmed this, that in progressive paraplegia due to compression or to intramedullary disease, the legs pass from the extended to the flexed condition, and it is generally recognized that paraplegia in flexion indicates very severe involvement of the cord.

As described by Babinski [7] it is characterized by the following features:—

(1) Muscular rigidity in flexion, which is intermittent and thus gives rise to involuntary movements of alternating flexion and extension, the former predominating.

- (2) Profound loss of voluntary power.
- (3) Diminution or absence of the tendon-jerks.
- (4) Exaggeration of the "defence reflexes" and an "extensor response."

Moreover, he says, in typical examples, examination of the cord reveals relatively slight secondary degeneration of the pyramidal tracts. On account of the absence of the tendon-jerks, which is in striking contrast to their activity in the extended form of spastic paralysis, he calls this type of spastic paralysis, "*cutanéoréflexe*," and the other "*tendinoréflexe*." This classification is misleading, and loses sight of the essential difference between the two conditions.

An analysis of the state of reflex activity of the two muscle groups in the limb—namely, the extensors and flexors—reveals the significant fact that the extensors show little or no reflex action, while the flexors show a high degree of reflex activity.

In the extensors we find no tone, the knee- and ankle-jerks are greatly diminished or actually absent, and there is no clonus.

In the flexors we find an extreme degree of reflex activity; the leg is flexed, and it requires considerable force to overcome the spasm, which, however, is notably intermittent, and has not the tonic character seen in the extensors in the extended form of spastic paralysis. Spontaneously, or on the lightest cutaneous or deep stimulus to the limb, strong flexor spasms occur; each of these being, as I have shown, a complete flexion reflex. Percussion of the tendons of the hamstrings gives invariably a brisk tendon-jerk, a significant fact in view of Babinski's description of the condition.

The essential feature of this form of spastic paralysis is that in it only the flexors retain any reflex activity, the extensors showing little or none. Whereas a lesion of the pyramidal tract alone produces a state of increased activity of both flexor and extensor muscles in the limb, the lesion in these cases has in addition destroyed all signs of reflex action in one group of muscles, leaving that of the other great group unaffected, and even increased since it is no longer antagonized. The two reflex systems are *differently* and *separately* affected. The analogy between this condition and that of the spinal animal is at once apparent.

A consideration of the character of the lesions giving rise to this condition shows that they are of several clinical and pathological types, but they have in common their severity, the fact that they are spinal in localization, and that they interrupt, more or less completely, conduction between the cord and the brain.

Short of actual total transverse lesion, the more complete the separation between ventral horn cells and brain, the more highly developed is this form of spastic paralysis.

The point raised by Babinski that there may be little or no descending pyramidal degeneration on pathological examination of the cord in such cases, has no special significance, for, as Gordon Holmes [23] has shown, there is no constant direct relation between the severity of the clinical manifestations and the secondary descending degeneration. A focal lesion of the cord may cause extreme spastic paralysis and loss of sphincter control, and yet, on autopsy there may be no descending pyramidal degeneration.

Since a lesion confined to the pyramidal tract never produces paralysis in flexion, we may assume that, as in the spinal animal, the interruption of an extrapyramidal path is an essential condition of its development. The fact that this form of spastic paralysis is seen in spinal lesions at the highest levels proves that this motor path must arise at a higher level than the cord, while its non-occurrence in cerebral lesions proves, similarly, that its origin must be at a lower level than that of the fore-brain. We are compelled, therefore, to assume the existence of an efferent motor path, other than the pyramidal tract, passing to the extensor muscles, or rather to their ventral horn cells, and to these alone.

It will be seen that the analogy between the state of reflex activity in the hind limb of the "spinal animal," and that of the lower limb of man in paraplegia in flexion, is as close as that between "decerebrate rigidity" and paraplegia in extension.

It would appear, therefore, that, as in animals, we have in man two separate systems of innervation of the limb musculature, each employing a definite group of muscles and giving rise in each of these to a specific form of activity, tonic in the one, clonic, or phasic, in the other.

The extensors need, for the maintenance of their hypertonus, the integrity of a reflex arc passing from the muscles themselves to a reflex centre in the grey matter of the brain-stem, probably the paracerebellar nuclei. The efferent limb of the arc consists of an extrapyramidal tract passing thence to the ventral horn cells of the extensor muscles.

The reflex activity of the flexors, on the other hand, is unaffected by the interruption of this path to their antagonists, and we must conclude that their reflex arc is purely spinal.

Recent investigations tend more and more to emphasize the important part played by extrapyramidal motor paths.

Foerster [22], v. Monakow [32], and Rothmann [35] attribute some of the phenomena of spastic paralysis to the taking over of the functions of the impaired pyramidal system by phylogenetically older motor systems, such as the rubro-spinal; and more recently the valuable work of Kinnier Wilson [42] has shown, in the most striking manner, the physiological possibilities of these paths.

While, however, the view attributing important functions to motor paths other than the pyramidal system is one widely held and strongly supported by clinical and pathological evidence, it has not been previously suggested that such a motor system may show a selective innervation of one group alone of the limb muscles.

Yet, Jackson's idea of the motor innervation of muscles "having the most tonic, the most confluent movements" by a special nervous mechanism differing from that innervating those muscles having "the most changing movements" is a distinct foreshadowing of the conditions of reflex action found to obtain in animals by Sherrington, and not less of the parallel state of affairs my observations show to exist in man.

The view advanced here of the tonic innervation of the extensor group of muscles in the lower limb by an extrapyramidal projection system, in addition to its cortico-spinal innervation by the pyramidal system, the flexors of the limb having an innervation by this latter system alone, harmonizes with the speculations of Jackson and experimental findings of Sherrington.

The conception of the lower motor neurone (the "final common path" of Sherrington) receiving impulses from more than one efferent projection system ("internuncial common paths") has been developed by Sherrington, and the double innervation of the extensor muscles of the lower limb provides a striking example of this factor in the co-ordination of reflex action.

Another phenomenon, which I have observed in a case of disseminated sclerosis, points to the existence of a grouping of the nervous representation of the limb muscles into extensor and flexor in the pyramidal tract itself.

The case was in every respect typical, and in history the patient stated that his right leg was much weaker than the left. Examination revealed the following condition: Both legs lay extended and adducted; passive movement revealed considerable spasticity in the extensors of both limbs, equal on the two sides. In power the extensors of both sides showed a slight and equal defect. The flexors, on the other hand, were very unequally affected. On the right they were extremely weak

and very little voluntary power of dorsiflexion of the foot or toes was present. On the left side flexion and dorsiflexion were normal. The tendon-jerks on both sides were brisk, and ankle-clonus was present.

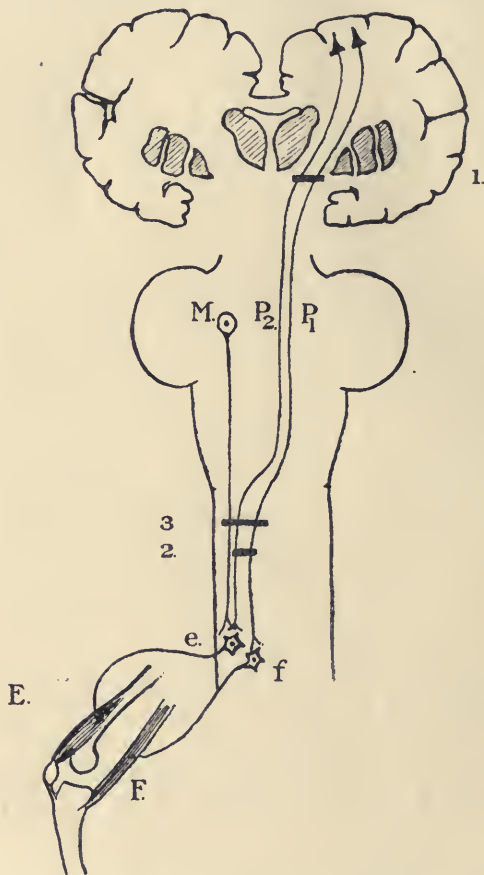


FIG. 12.—In this diagram P₁ and P₂ are pyramidal fibres going to *e* and *f*, the ventral horn cells of extensor and flexor muscles respectively. E and F represent these muscles. M is the extra-pyramidal path arising probably in connexion with the paracerebellar nuclei and going to the extensor neurone.

A lesion, 1, gives rise to a paralysis of the extended type. Reflex activity of both groups of muscles is increased.

A lesion, 2, a lateral sclerosis, produces the same result. Both involve the pyramidal system alone.

A lesion, 3, besides interrupting the pyramidal tract, involves the extrapyramidal path also, and in such a case paralysis in flexion results.

The plantar response on the right side was "extensor," on the left a normal flexor was obtained and no trace of a pathological plantar reflex was to be found, nor any reflex flexion of the limb.

According to my view, pyramidal fibres to the flexors and extensors in the right leg were equally involved. On the left side, on the other hand, pyramidal fibres to the flexors were intact, only those to the extensors being involved. Hence, on this side there was a normal plantar response.

Examples of spastic legs with increased jerks, clonus, and a normal plantar response, are familiar to all neurologists, and would repay closer observation from this point of view.

Current theories do not allow the existence of any grouping of fibres in the pyramidal tract — either physiological or anatomical. However, the observation above recorded points to a physiological grouping, and further investigations are necessary to elucidate this question.

The foregoing diagram represents the hypothesis of the motor innervation of the limbs, which I put forward (fig. 12).

§ 3.—*Total Lesions of the Cord.*

In comparing the condition of paraplegia in flexion with that of the hind limbs in the spinal animal, it is necessary to bear in mind the clinical picture of complete transverse spinal cord lesion in man.

As Bastian [9] first pointed out, in this condition there is complete flaccid paralysis with absence of the tendon-jerks, and complete sensory loss. There are also sphincter defects, and rapid wasting and degeneration of the muscles sets in. Occasionally, according to Collier [15], certain skin reflexes are present in reduced degree, and constitute the sole evidence of self action in the limb.

This clinical picture is often seen transiently following some severe and acute cord lesion, such as occurs in fracture dislocation of the spine or in acute transverse myelitis. In such cases partial recovery ensues, but before this appears we can regard the condition as one of complete physiological transverse lesion of the cord.

Therefore, although the condition of paraplegia in flexion may present many points in common with the condition of the hind limbs of the spinal animal, it is clear that it differs widely from the clinical picture presented by the leg in complete cord lesions in man, i.e., in the "spinal" man. This difference, however, is only one of degree, as a study of recorded cases and my own observations show.

Sherrington has pointed out that following spinal transection, a condition of "spinal shock" ensues. This affects mainly the extensors,

and the flexors but slightly and transiently. Yet while the rabbit recovers almost completely from spinal shock in a few hours, the dog recovers more slowly and less completely, while higher animals, like the monkey, only show long delayed and partial recovery. In the spinal rabbit, a knee-jerk reappears in a few hours, while in the monkey it may not be elicitable for months. Sherrington considers this shock to be due to the rupture of certain efferent paths arising in the brain-stem and also to the phenomenon of "isolation dystrophy": that is, to trophic degenerative changes in the nervous elements when cut off from efferent impulses from the brain.

Man differs from the lower animals only in that, in him, spinal shock is more intense, and that the phenomena of shock are perpetuated by the occurrence of actual degenerative changes in the nervous elements themselves, which naturally destroy all function in the isolated cord.

Moreover, Sherrington has observed that protective reflexes, or as he calls them "nociceptive reflexes" are relatively little depressed by spinal shock, and are the reflex phenomena which emerge earliest from this condition. The flexion reflex of the hind limb affords an excellent example of this.

He says: "In the monkey and in man spinal shock is not only peculiarly intense but peculiarly long lasting. The withdrawal from the isolated cord of influences it is wont to receive from centres further headward may induce an alteration of trophic character in spinal cells—an 'isolation dystrophy'—visible, it may be, as Nissl's chromatolysis.

"This 'isolation dystrophy' ensuing on shock would add itself as a longer lasting, in some elements, perhaps, a permanent, depression. . . . The deeper depression of reaction into which the higher animals as contrasted with the lower sink when made 'spinal' appears to be significant of this, that in the higher types, more than in the lower, the great cerebral senses actuate the motor organs and impel the motions of the individual."

When we come to analyse the "skin reflexes," which are preserved in cases of complete transverse cord lesions, we find them to consist in minimal forms of the flexion reflex, which I have described. In other words, there is retained in a depressed form the great protective or "nociceptive" reflex of the limb. It is further to be noted that this reflex involves the activity of flexor muscles only.

A case of complete traumatic division of the spinal cord by a bullet

wound in the dorsal region is recorded by Lewandowsky and Neuhof [27]. It bears out the view I have advanced.

For a period of several days following the lesion, before degenerative changes had set in in the muscles, an "extensor response" was obtained together with "reflex contractions of certain of the thigh muscles."

These reflex phenomena were increased in facility and intensity by prolonged faradization of the limb, and a transient ankle-jerk but never a knee-jerk, was also obtainable by these means. However, the most active and enduring reflex seen was the Babinski plantar response. This establishes the occurrence of a flexion reflex in the "spinal" man.

I have personally observed three cases of physiologically complete cord lesion, one within twenty-four hours of a fracture dislocation of the dorsal spine. The legs were flaccid, powerless, and absolutely insensitive, all tendon-jerks were absent and there was retention of urine. Stroking of the sole gave as response a visible contraction of the hamstring and of tensor fasciæ femoris. Twenty-four hours later a dorsiflexion of foot and feeble flexion of the knee and hip were obtained, and on some occasions an actual "extensor response" was obtained, but tired readily. At the moment of writing—six days after the trauma—the condition present is unchanged, but muscular wasting has appeared.

Another case seen seven days after the onset of an acute transverse myelitis gave an identical result. This case is recorded at length in the Appendix, and affords a striking example of the progressive evolution of reflex activity in a spinal cord recovering from physiologically complete section.

Even accepting the presence of a flexion reflex in the lower limbs of the "spinal" man, it has to be admitted that the condition of flaccid paralysis with depressed reflex activity differs widely from that of paraplegia in flexion. However, the difference is merely one of degree, in that in the latter the flexors show not a minimal but a maximal amount of reflex activity. In no other respect is there any essential difference. Still, how is this difference to be explained?

Dejerine [17] refuses to regard the flexion reflex as evidence of spinal function liberated from cerebral control, as Marie and Foix suggest when they call the phenomenon a "*Réflexe d'automatisme médullaire*," because, he says, it only occurs in incomplete destruction of the cord, and never when transection is absolute. This, as I have shown, is not strictly true. It is true, however, that these reflex phenomena are most marked when the separation of cord from brain is incomplete. To this we may add that the more profound the interruption is, short of

complete section, the more marked are these reflexes. The condition of paraplegia in flexion is evidence of this.

It must be admitted that in the condition of disease in which we have to study these reflexes in man the lesions are brutal and incomplete, and we seldom have exact knowledge of their extent.

I would suggest that in the condition of paraplegia in flexion we have the "spinal" man without the phenomena of "spinal shock" or "isolation dystrophy." It is the final separation of cord from brain that induces these phenomena and depresses at first, and finally destroys the reflex activity of the flexors.

In paraplegia in flexion, according to this view, there is complete liberation of spinal reflex function without that depression of reaction and subsequent destruction of nervous elements which anatomically complete division produces.

The presence of a very depressed, minimal flexion reflex during the short period before degenerative changes ensue in nerve and muscle, in cases of complete cord transection in man, is definite evidence that there is no essential qualitative distinction between the condition of paraplegia in flexion and that of the flaccid paralysis seen in the latter circumstances, and strongly supports the view that these two clinical pictures differ merely in the presence in one of them of "spinal shock."

To sum up, we may say that there is strong evidence that the condition of paraplegia in extension, including here that of the lower limb in hemiplegia, is analogous with the "decerebrate rigidity" of animals deprived of their hemispheres: that paraplegia in flexion and the flaccid paralysis of complete cord transection in man differ only in degree, and are analogous with the condition of the hind limb of the "spinal animal."

In paraplegia in extension both extensor and flexor groups of muscles show a high degree of involuntary reflex activity, and this is specific in character for each group.

In paraplegia in flexion and in the flaccid paralysis of the complete cord lesion the flexor muscles alone show any sign of reflex action.

Since these two reflex mechanisms can be thus separately affected, they must be differently represented in the central nervous system; that is, there are two systems of motor innervation of the limb musculature.

In any lesion of and confined to the pyramidal system, we find both these reflex systems constantly active, i.e., we see the extended form of spastic paralysis of the leg, and never the form with contracture in flexion. A lesion producing this is always spinal, and must involve the interrup-

tion of some efferent path in the cord, other than the pyramidal tract, since this is already involved; I say efferent paths, since the condition of paraplegia in flexion may be found with an intact afferent system.

This further involvement of an extrapyramidal path affects only the extensors, and integrity of this path appears to be essential if these muscles are to display any reflex action. The centre from which it arises is, I conclude, analogous with that "prespinal centre" for the extensor muscles in animals for the existence of which Sherrington has brought forward convincing evidence.

I hope to demonstrate, in a subsequent paper, that the phenomena of spasticity and contracture, which have been the subject of much recent work by Foerster, are also capable of complete explanation in accordance with the hypothesis here advanced.

CHAPTER VI.—GENERAL SUMMARY.

(1) The reflex movements of the lower limbs in spastic paralysis are almost entirely movements of flexion of the limb. With flexion is included dorsiflexion of foot and toes, more especially the hallux.

These movements occur, apparently spontaneously, as the well-known flexor spasms seen in certain cases of paraplegia, and also on appropriate stimulation of the limb. This reflex I have called the flexion reflex of the lower limb.

(2) The "receptive field" of this reflex commonly includes the whole limb, skin and deep structures, except for a small portion of the proximal part. The reflex is not purely cutaneous. The form of stimulus most effective is that having a nocuous or harmful character, but light painless stimuli applied to the distal extremity of the limb, the sole, suffice to induce the reflex. The muscles actuated are the flexors and dorsiflexors of the limb, and the reflex response is a simple movement of flexion at all the joints.

(3) Of this reflex flexion, dorsiflexion of the hallux is an integral and inseparable part, and this constitutes the "extensor" type of plantar response, the Babinski toe phenomenon, the appearance of which is recognized to be pathognomonic of pyramidal tract affection.

The "extensor response" is, therefore, part of the flexion reflex, and analysis proves it to be an integral part of this, never occurring without reflex contraction of the proximal limb flexors.

(4) The physiological significance of the flexion reflex is that of a defensive reflex, and it has no relation to "spinal stepping."

(5) Concurrently with contraction of the limb flexors in this reflex is inhibition of their antagonists, and all the phenomena of "reciprocal innervation" are seen in the reflex.

(6) Accessory to this reflex is reflex extension of the crossed limb which, following Sherrington, I call the crossed extension reflex. This includes plantarflexion of foot and toes, "the crossed plantar reflex" of many authors. This is shown to differ from the normal flexor plantar reflex.

(7) The study of spastic paralysis of the lower limbs, from the point of view of reflex movement, confirms the existence of two clinical types. These have been described by Babinski as "paraplegia in extension" and "paraplegia in flexion."

I have pointed out here that the essential difference between the two types is that, while in the extended form of spastic paralysis of the lower limbs both extensor and flexor groups of muscles are in a state of heightened reflex activity in the flexed spastic leg, only the flexors retain this, the extensors showing diminished or absent reflex action.

(8) The reflex activity of these two groups of muscles is, it is here put forward, of specific type in each case. The extensors show a maintained tonic reflex—the spasticity of the extended leg. This may be called a static reflex. The flexors show, characteristically, reflex action of phasic type, which gives rise to reflex movements.

(9) In a cerebral lesion or in a purely pyramidal tract affection, however complete, we see constantly the extended type of spastic paralysis in the legs.

The type of spastic paralysis in flexion, or, as it has with scant appreciation been called, "spastic paralysis with flexion contracture," is only seen in spinal cord affections; most commonly in severe, diffuse lesions, never in pure lateral sclerosis involving only the pyramidal tracts.

To produce this condition the interruption of an efferent tract in the cord other than the pyramidal tract is essential. This path arises caudal to the fore-brain and probably in the pons, in connexion with the paracerebellar nuclei.

The effect of a lesion of this extrapyramidal motor path is to abolish the reflex tone in the extensor muscles, without affecting the reflex activity of the flexor muscles.

(10) The condition of paraplegia in flexion is an example of unantagonized flexor reflex action, and it shows intermission, due to the phasic nature of this, until permanent contracture ensues.

Since the condition is found in the severest spinal lesions, the reflex

activity of the flexors may be considered purely spinal in origin and not dependent on any efferent path from the brain.

(11) In complete spinal transection, physiological or anatomical, the reflex activity of the limb is almost completely absent. But a minimal flexion reflex persists on stimulation of the sole, and thus affords further evidence of the purely spinal nature of this reflex. The extensors show no reflex activity in these cases.

(12) The condition of flaccid paralysis of the limbs in complete lesions of the spinal cord differs, therefore, in degree only from that of paraplegia in flexion, which I conclude is analogous to the condition of the hind limbs of the "spinal animal." In complete spinal lesion the phenomena of "spinal shock" and "isolation dystrophy" mask and finally abolish the reflex activity of the flexors.

(13) It will be seen from this that there is a double system of motor innervation of the lower limbs, such as was first suggested by Jackson and verified experimentally in animals by Sherrington.

I have endeavoured to show further that the two factors in this are, first, the pyramidal system which innervates both limb flexors and extensors. A lesion of this path liberates both reflex systems from control, and in the limb extensors we see the extended form of spastic paralysis.

The second component is a tonic innervation along an extrapyramidal tract arising in the brain-stem and passing to the extensor muscles only. Interruption of this abolishes the reflex activity of these muscles, leaving that of the flexors unimpaired. The condition of spastic paralysis in flexion then ensues, the reflex action of the flexors being purely spinal.

(14) An analysis of the phenomenon of spastic paralysis of the limb extensors in man demonstrates the close analogy existing between the physiological principles of motor innervation in animals and in man.

APPENDIX I.

ILLUSTRATIVE CASES.

CASE 1.—*An instance of physiologically complete cord lesion. Flexion reflex present in minimal form, no other reflexes present. Slow recovery during which the legs passed from complete flaccid paralysis through a condition of paraplegia in flexion to that of paraplegia in extension, with corresponding changes in the reflexes.*

F. T., a girl, aged 19, was admitted into the National Hospital under the care of Dr. Batten on February 2, 1914. Eight days before admission she began to develop a rapidly progressive paraplegia, which became complete on the

second day. For six days previous to examination, there had been complete flaccid paralysis with sensory loss and retention of urine.

Condition on February 2. There was absolute flaccid paralysis of both lower limbs, which lay extended and rotated out. They were absolutely devoid of tone. On attempting to sit up in bed the umbilicus moved up. There was absolute loss to all forms of sensibility below a line drawn round the trunk one inch above the umbilicus. There was retention of urine. All tendon-jerks were absent. The faradic excitability of the muscles was good, though they were readily fatigued.

The Flexion Reflex.—Light stroking of the sole, but no form of stimulation of any other part of the limb, gave a quick contraction of the hamstrings and of the anterior tibial muscles. There was slight flexion of the knee and hip without movement of the toes, but a feeble dorsiflexion of the foot. If the stimulus to the sole was very light it was possible to get a motor response limited to a palpable contraction of semitendinosus and semimembranosus, but too weak to produce any movement of the limb. Whenever the reflex contraction appeared in the muscles distal to the knee, it was well marked in all the proximal flexors. That is, the minimal response was in the proximal muscles. Pin-prick on the sole gave similar results.

Strong faradism applied to the muscles directly by means of needle electrodes for periods of from ten to thirty minutes had no effect either on the flexion reflex or the tendon-jerks.

On February 4. No change, except that to intense stimulation of the sole the small toes dorsiflexed feebly, but there was no movement of the great toe. No further change till February 8. The limbs now showed general wasting, and faradic excitability was somewhat reduced.

February 10. All the tendon-jerks were absent, but percussion over the heads of the metatarsals gave reflex flexion of the limb. The flexion reflex was facile from the sole. The minimal response was contraction of the hamstrings and of tensor fasciæ femoris. To stronger stroking of the sole there was added to flexion at hip and knee dorsiflexion of ankle and of all the toes; a good "extensor response." If the dorsiflexion of the foot was resisted the "extensor response" was more ample. The receptive field was still confined to the sole for all forms of stimuli. Strong faradism for a period of thirty minutes was devoid of result.

February 12. Light stroking of the sole now gave a typical "extensor response," accompanied in every case by visible limb flexion. Successive stimulation soon tired the reflex, the response disappearing first distally—i.e., in the toe, and then in the ankle. So that finally a stimulus previously able to evoke a complete reflex now only gave flexion at hip and knee. Oppenheim's procedure for the first time gave a feeble contraction of the proximal flexors, but no toe movement. The motor and sensory condition of the limbs had not changed, and the tendon-jerks were absent.

February 13. The flexion reflex as before. The knee- and ankle-jerks were absent, but now percussion of the tendons of semitendinosus and semimembranosus gave a feeble, palpable contraction of these muscles.

February 17. Knee- and ankle-jerks absent, but hamstring-jerks brisk on both sides. The flexion reflex could now be elicited in complete form by light stroking of the sole, and by pin-prick of the skin up to the level of the calf. Also strong percussion of the shaft of the tibia and of the bony points round the ankle gave a flexion reflex complete in form. The minimal response was still in the hamstrings.

February 22. The tendon of biceps femoris now gave a jerk. Oppenheim's method also gave an "extensor response." The first sign of returning sensibility was seen in slight perception of the vibrations of a tuning-fork placed on the tibia. A complete flaccid paralysis remained.

At this time, twenty-six days from the date when the lesion became complete, the flexors showed rapidly returning reflex activity, but the extensors were still absolutely without any such activity. Flexor reflex activity was present from the first, when the lesion was physiologically complete.

March 8. Flexion reflex now obtainable by pin-prick of any part of the limb surface below the middle of the thigh. There was no trace of any crossed reflex response. *The knee-jerks were feebly present for the first time.* These appeared after some sensory return indicated that the lesion was no longer complete. Ankle jerks absent.

March 16. Knee- and hamstring-jerks present, ankle-jerks still absent. The flexion reflex was gaining in force and amplitude, and the receptive field was increasing in extent. Pin-prick of the lower part of the abdominal wall gave feeble reflex flexion, in which a toe movement was just perceptible. The "extensor response" was very ample and facile on light stimulation of the sole, but could not be obtained without contraction of the proximal flexors of the limb. Complete flaccidity remained.

During April practically no change occurred.

May 11 (thirteen weeks from onset). The legs lay half flexed, and when straightened slowly returned to this position, and there was now slight but definite tone in the hamstring muscles and in the hip flexors. Less definite hypertonus was felt in the knee extensors. Any sudden passive movement of the limbs caused a strong flexor spasm.

During May, June and July, strong flexor spasms began to appear, and the legs, although not powerfully flexed, always lay fully flexed, and sudden passive extension increased the spasm. The knee-jerk was still of poor facility, but the ankle-jerk did not appear. The flexion reflex was very facile to all forms of stimulation.

In August strong adductor spasm began to appear, and more evidence of spasticity in the extensors.

During September the flexor spasms abated notably and the patient began to remark that sudden extensor spasms came on and made the limbs very rigid in extension. Their attitude was now always one of extension.

In October, the ankle-jerk at last reappeared. There was now strong extensor rigidity and flexor spasms were occasional. The flexion reflex was as facile as ever, but the flexion was not so ample and a quick extensor rebound cut it short always.

In September the obturator nerves were crushed to overcome the adductor spasm. This it did completely.

Present condition (October 30).—The legs are very spastic in extension. All the tendon-jerks are brisk and there is ankle-clonus on both sides. There is feeble power of extension of the limb, but as yet scarcely power of flexion, except at the hip.

The flexion reflex is elicitable over a wide field and is ample and complete. The minimal response remains in the hamstrings and in tensor fasciæ femoris, but to any but the slightest stimulus a complete flexion reflex is obtained.

The return of sensation has been much more complete than that of power, and sensory loss is now only moderately marked to any form of sensibility.

This case is instructive from many points of view. It is of special interest here as showing the evolution of the reflex activity of the limb in the process of recovery from "spinal shock" in the first place and also in the clearing up of the lesion, which remained complete for some time according to accepted standards.

The order of appearance of the tendon-jerks is also of the greatest importance. They are seen in the hamstrings; the flexors, almost three weeks before their reappearance in the extensors. Further, in view of the work of Collier [15] and of Lewandowsky and Neuhof [27] on the effect of strong faradism on the tendon-jerks in cases of complete section of the cord, it is of interest to note that in this case frequent faradism appeared to have no effect in accelerating the appearance of the tendon-jerks.

Summarized, we have here a case of temporary physiological solution of continuity of the spinal cord, in which recovery has slowly and partially ensued. While the lesion was total and "shock" was profound, the flexion reflex was still obtainable from some of the muscles, in which it is present when complete, on stimulation of a small receptive field at the apex of the limb, the minimal motor response being in the muscles at the limb base. When fully developed the flexion reflex included flexion at hip and knee and dorsiflexion of ankle and of hallux—the "extensor" type of plantar reflex. This was inseparable from the flexion reflex; it was elicited by the same stimuli, but was evidently not the minimal response. *Pari passu* with the spread of reflex motor response the receptive field also spread until there was obtained from the whole surface of the limb and from most of its deeper structures, the same complete flexion reflex, in all respects identical with the nociceptive flexion of the hind limb of the spinal dog, described by Sherrington.

Further, this reflex response from the limb flexors was obtained

when the lesion was complete, at a stage when no reflex activity was seen in the extensors, and before the presence of the knee-jerk gave any evidence of reflex tone in the extensors. This only appeared after slight sensory return showed that the cord below the lesion was no longer completely separated from the higher centres.

CASE 2.—*An instance of progressive paraplegia passing from the extended condition to that of paraplegia in flexion, the limbs finally becoming flaccid. The dissolution of reflex activity in the lower limbs is seen. The case shows very well the differential effect of a progressive lesion of the cord on the reflex activity of extensor and flexor groups of muscles respectively.*

Percy G., aged 16, was admitted into the National Hospital, in April, 1914, under the care of Dr. Gordon Holmes. He gave a history typical of disseminated sclerosis: Diplopia, misty vision, unsteadiness of limbs and sphincter disturbances, dating from October, 1910. He was previously in hospital in October, 1911, when the diagnosis was made.

He remained fairly well until February of this year, when he had in rapid succession a series of epileptiform fits with vomiting, followed by progressive weakness of the limbs and other disturbances of the nervous system.

On examination in April, he was emotional and fatuous. He had diplopia and nystagmus with left-sided facial weakness. Speech was syllabic and slow. The upper limbs were spastic and unsteady, the left showed some loss of the sense of position.

The lower limbs lay extended and adducted; both showed moderate extensor spasticity, but power was almost completely absent. There was no sensory loss. The tendon-jerks were all brisk, patellar- and ankle-clonus were present at times. Percussion of the sole gave a knee-jerk (Loewy and Cohn).

A facile flexion reflex was present and could be obtained from the whole limb and from the perinæum.

Light stroking of the sole and dorsum of the foot gave a complete flexion reflex. The minimal stimulus gave a visible flexion of the limb, and an "extensor response" could not be obtained without this contraction of the proximal limb flexors. Pin-prick over the whole limb gave a complete reflex. Squeezing of the calf or thigh muscles gave a good reflex.

From whatever part of the limb obtained, and by whatever form of stimulus, the reflex response was unvarying limb flexion with dorsiflexion of foot and hallux.

Accompanying the flexion reflex was a crossed extension reflex. If the crossed limb were previously flexed, this consisted of extension at hip and knee, with plantarflexion of foot and all the toes. The movement was quick and forcible. If the crossed limb lay fully extended the crossed reflex consisted of plantarflexion of the foot and toes (see figs. 8A and 8B).

The reflex flexion of the homolateral limb was soon cut short by a quick extensor rebound, while the crossed extension showed a flexor rebound (fig. 8C). The graphic record shows all these phenomena (fig. 9).

This condition remained more or less unchanged until May 5, when the right leg was noticed to lie often in an attitude of flexion, to which it soon returned when passively extended.

Examination now revealed the following condition. Voluntary power was gone on both sides. The right leg was flaccid, but showed possibly slight tone in the hamstrings. The left leg was much as on admission.

The right knee- and ankle-jerk were absent, those on the left were brisk. The hamstring-jerks were brisk on both sides, especially on the left. The flexion reflex was facile on both sides and had not changed in any way, except that the right no longer showed any extensor rebound, while the left flexion reflex was not accompanied by any crossed extension. The right flexion reflex was so accompanied.

In other words, the extensor group of muscles of the right leg had lost their reflex activity, while that of the flexors was not changed.

However it was repeatedly noticed on this and the few following days that if, while percussing the right patellar tendon, the left flexion reflex were strongly elicited, a feeble knee-jerk could be obtained. *The left flexion reflex was reinforcing the extensors of the opposite limb.*

May 7. The right leg now lay continually flexed and the reflexes were as before. The left leg was still rigid in extension and the reflexes unchanged. The hamstrings of the right leg were now developing a condition of tone upon which frequent flexor spasms were superimposed, and any sudden passive extension of the limb provoked a strong increase of the flexor spasm, including an "extensor response." The limb was also wasting generally, more than the left.

Crossed extension of the left limb persisted till the end of May, when the left limb also went into flexion and lost its knee- and ankle-jerks. Crossed extension of this limb on stimulating the right sole now disappeared finally.

The hamstring-jerks on both sides remained brisk.

Both limbs had now lost the reflex activity of their extensor group of muscles, and the condition of paraplegia in flexion was present. The flexor spasms of both legs were frequent and the flexion reflex was very facile, but the minimal response was now seen to be in the hamstring muscles on light stimulation of the sole. At first the minimal response had consisted in a complete reflex.

From this date the reflex activity of the limbs declined rapidly, until finally only a feeble flexion could be obtained from the sole, and from no other part of the limb. The minimal response was seen very clearly in the proximal limb flexors and shortly before death stimulation of the sole evoked only this response.

Autopsy confirmed the diagnosis and the cord showed almost complete sclerosis in the dorsal region, only a small area in one ventrolateral column staining by the Weigert method.

This case shows the phenomena observed in Case 1, but inversely. It confirms the views formed as to the nature of the flexion reflex from

the study of that case. It shows the decline of the reflex activity of the extensor muscles of the limb at a time when that of the flexors was unaffected, and affords strong evidence of the existence of two systems of motor innervation of the limb musculature.

APPENDIX II.

GRAPHIC METHODS.

The method employed was the direct recording on a revolving drum of the limb movements. In cases where these were of too great amplitude, the thread from the limb passed to the outer circumference of a light multiple wheel such as is used in the kymographs of the physiological laboratory. From a smaller circumference on the same wheel a thread passed to a recording lever.

The graphic recording of the reflex movements of the spastic limbs offers considerable difficulties. The sudden occurrence of strong flexor spasms continually pulls the recording lever off the surface of the revolving drum and even breaks the connecting thread. In many cases repeated efforts were necessary before a presentable record could be obtained. In the course of making records from such cases, one was struck by the continually changing degree of the reflex activity of the spastic limbs. Particularly did this seem the case with the extensor muscles. The hypertonus, the briskness of the tendon-jerks, and the occurrence of clonus altered from moment to moment. The flexion reflex showed much less variation.

To record movements of the whole limb or of the hallux alone, a thread is attached to the tip of the great toe by a piece of adhesive strapping. To record limb flexion apart from toe movement the writing lever is connected with the internal malleolus in the same manner. Either direct or proportional recording can be used.

A metronome connected in circuit with an electric signal is used to record time in seconds.

A record of the time relations of the knee-jerk or of the plantar stimulation in the flexion reflex can be obtained very simply, and does not necessitate the elaborate apparatus described in "Lewandowsky's Handbuch" and elsewhere.

A piece of metallic gauze, such as is used in electro-therapy, is wound round the knee over the patellar tendon. A similar piece is wound round the percussion hammer. Wires lead from each to a

circuit in which are a battery and an electric signal. On striking the patellar tendon, contact is at once made and recorded by the signal on the smoked surface of the kymograph.

In the accompanying diagram (fig. 13) the two alternative methods of direct (D) and proportional (E) recording of limb movement are indicated.

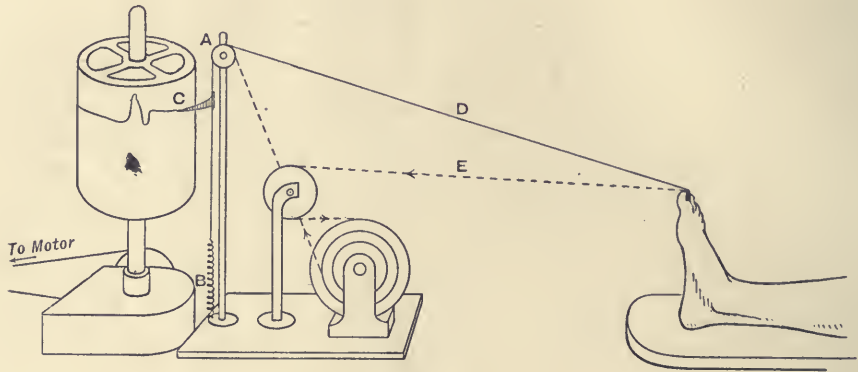


FIG. 13.

The thread in each case passes over a wheel, A, and is fastened to a spring, B. This keeps the thread taut and prevents it from becoming loose in the sudden flexion or extension movements of the limb. The recording lever, C, is fastened to the thread, and consists of a piece of parchment paper.

The drum is revolved at given speeds from a small motor.

The electric signal is not represented.

REFERENCES.

- [1] BABINSKI. "Du phénomène des orteils et de sa valeur sémiologique," *Semaine Médicale*, 1898, p. 321.
- [2] *Idem*. "Sur une forme de paraplégie spasmodique consécutive à une lésion organique et sans dégénération du système pyramidal," *Bulletins, etc., des Hôpitaux de Paris*, 1899, p. 342.
- [3] *Idem*. "Sur la transformation du régime des réflexes cutanés dans les affections du système pyramidal," *Rev. Neurol.*, 1904, No. 1, p. 58.
- [4] *Idem*. "Sur le réflexe cutané plantaire," *ibid.*, 1907, No. 14, p. 755.
- [5] *Idem*. "Paraplégie spasmodique organique avec contracture en flexion et contractions musculaires involontaires," *ibid.*, 1911, No. 2, p. 132.
- [6] *Idem*. "Modifications des réflexes cutanés sous l'influence de la compression par la bande d'Esmarch," *ibid.*, 1911, vol. ii, p. 951.
- [7] *Idem*. "Contracture tendino-réflexe et contracture cutané-réflexe," *ibid.*, 1912, No. 14, p. 77.

- [8] BABINSKI. "Réflexes tendineux et réflexes osseux," Paris, 1912, p. 64 *seq.* Reprinted from *Bulletin Medical*, October—November, 1912.
- [9] BASTIAN. "On the Symptomatology of Total Transverse Lesions of the Spinal Cord, with Special Reference to the Condition of the Various Reflexes," *Med. Chir. Trans.*, 1890, vol. lxxii, p. 151.
- [10] BEEVOR. "Ueber die Koordination und Repräsentation der Muskelbewegungen im zentralen Nervensystem," *Ergebnisse der Physiologie*, 1909, 8 Jahrgang, S. 326.
- [11] BROWN-SÉQUARD. "Sur l'arrêt immédiat de convulsions violentes par l'influence de l'irritation de quelques nerfs sensitifs," *Archives de Physiologie*, 1868, vol. i, p. 157.
- [12] BYROM BRAMWELL. "Note on the Crossed Plantar Reflex," *Rev. Neurol. and Psychiat.*, 1911, vol. ix, p. 49.
- [13] CHARCOT. "Lectures on Diseases of the Nervous System," New Sydenham Society's Translation, 1881, vol. xc, p. 93.
- [14] CLARKE and HORSLEY. "On the Intrinsic Fibres of the Cerebellum, its Nuclei and its Efferent Tracts," *Brain*, 1905, vol. xxviii, p. 13.
- [15] COLLIER. "The Effects of Total Transverse Lesion of the Spinal Cord," *Brain*, 1904, vol. xxvii, p. 38.
- [16] DEJERINE et VALENSI. "Paraplégie cervicale d'origine traumatique. Ecrasement de la moëlle épinière, etc.," *Rev. Neurol.*, 1911, No. 14, p. 141.
- [17] DEJERINE et LONG. "Examen histologique d'un cas de section complète de la moëlle cervicale inférieure d'origine traumatique," *Rev. Neurol.*, 1912, No. 24, p. 769.
- [18] DEVIC et GALLAVARDIN. "Sur un cas remarquable de contracture post-hémiplégique," *Rev. Neurol.*, 1903, No. 2, p. 53.
- [19] FAIRBANKS. "The Contralateral Plantar Reflex," *Rev. Neurol. and Psychiat.*, 1911, vol. ix, p. 225.
- [20] FOERSTER. "Die Kontrakturen bei den Erkrankungen der Pyramidenbahn," Berlin, 1906.
- [21] *Idem.* "Relations between Spasticity and Paralysis in Spastic Paralysis," Seventeenth International Congress of Medicine, London, 1913, Section XI, Neuropathology, vol. ii, p. 55.
- [22] *Idem.* "Das phylogenetische Moment in der spastischen Lähmung," *Berlin. klin. Wochenschr.*, 1913, Nos. 26 and 27, S. 1255.
- [23] HOLMES, GORDON. "On the relation between loss of Function and Structural Change in Focal Lesions of the Central Nervous System, with special reference to Secondary Degeneration," *Brain*, 1906, vol. xxix, p. 514.
- [24] HORSLEY. "The Functions of the Cerebellum," *Brain*, 1906, vol. xxix, p. 446.
- [25] HUGHLINGS JACKSON. "Remarks on Rigidity of Hemiplegia," *Medical Examiner*, April, 1877, p. 271.
- [26] LEWANDOWSKY. "Handbuch der Neurologie," Berlin, 1913, Bd. 1, t. ii, S. 696.
- [27] LEWANDOWSKY und NEUHOF. "Über Wiederbelebung der Reflexe nach Rückenmarksverletzung," *Zeit. f. d. gesamte Neurol. und Psych.*, 1912, Bd. xiii, S. 444.
- [28] LOEWY. "Die plantare Reflexzone für den M. quadriceps," *Neurol. Centralb.*, January, 1913, S. 90.
- [29] MANN. "Über den Lähmungstypus bei der cerebralen Hemiplegie," *Volkman's klinische Vorträge*, 1895, Inn. Med., No. 39, Nos. 30-54, S. 355.
- [30] MARIE et FOIX. "Les réflexes d'automatisme médullaire," *Rev. Neurol.*, 1912, vol. xxiii, p. 657.
- [31] *Idem.* "Réflexes d'automatisme médullaire et réflexes dits de défense. Le phénomène des raccourcisseurs," *Semaine Médicale*, October 22, 1913, p. 505.
- [32] v. MONAKOW, "Gehirnpathologie," Wien, 1897.
- [33] NOICA. "Sur les Réflexes cutanés du dos," *Rev. Neurol.*, 1912, vol. xxiii, p. 134.
- [34] OPPENHEIM. "Lehrbuch der Nervenkrankheiten," Berlin, 1913, 6te Aufl., Bd. ii, S. 896.
- [35] ROTHMANN. "Restitutionsvorgänge bei cerebralen Lähmungen, &c.," *Deutsch. Zeitschr. f. Nervenheilk.*, 1914, Bd. 1, S. 406.

- [36] SHERRINGTON. "The Integrative Action of the Nervous System," London, 1906.
 - [37] *Idem.* "Flexion Reflex of the Limb, Crossed Extension Reflex, and Reflex Stepping and Standing," *Journ. of Physiol.*, 1910, vol. xl, p. 28.
 - [38] *Idem.* "Remarks on the Reflex Mechanism of the Step," *Brain*, 1910, vol. xxxiii, p. 1.
 - [39] STROHL. "Les réflexes d'automatisme médullaire: Le phénomène de raccourcisseurs," *Thèse de Paris*, 1913.
 - [40] THIELE. "On the Efferent Relationship of the Optic Thalamus and Deiters' Nucleus to the Spinal Cord, with special reference to the Cerebellar Influx of Hughlings Jackson and the Genesis of the Decerebrate Rigidity of Ord and Sherrington," *Journ. of Physiol.*, 1905, vol. xxxii, p. 358.
 - [41] VAN GEUCHTEN. "Réflexes cutanés et Réflexes tendineux," *Rev. Neurol.*, 1900, vol. viii, p. 736.
 - [42] WILSON, KINNIER. "Progressive Lenticular Degeneration, &c.," *Brain*, 1912, vol. xxxiv, p. 296.
 - [43] WOERKOM, v. "Sur la signification physiologique des réflexes cutanés des membres inférieurs," *Rev. Neurol.*, 1912, vol. ii, p. 285.
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PUBLICATIONS RECENTLY RECEIVED.

[Notes on a book under this heading do not preclude a subsequent review.]

Die funktionellen und hirnanatomischen Befunde bei der japanischen Tanzmaus. Von Dr. TACO KUIPER. S. 154, with many plates under separate cover. Rotterdam: Hengel, 1913.

This admirable monograph is founded on the microscopical study of the brains of five fully grown and four newly born dancing mice. After a clear summary of previous work the author gives his own observations. He believes that the movements performed by these extraordinary animals vary greatly; some resemble "forced" movements, some are more like attacks of "whirling," whilst other mice carry out definite dancing evolutions. The animals differ greatly in liveliness and force, and the loss of general muscular tone varies in extent. All his animals were undoubtedly deaf. The lesion is a degeneration of the whole system of the eighth nerve ["Octavus-system"] including both its peripheral and central endings. The plates are excellent.

Les Réflexes d'Automatisme médullaire, le Phénomène des Raccourcisseurs. [Travail du Service et du Laboratoire de M. le Professeur Pierre Marie]. Par Le Docteur ANDRÉ STROHL. Pp. 164. Paris: Steinheil, 1913.

In this thesis Dr. Strohl set himself to review the path of the different reflexes in man and to investigate in particular that pathological group attributed by Marie and Foix to spinal automatism. He follows these authorities in believing that the knee-jerk is a true reflex, and that, when the cerebrospinal conduction is diminished or destroyed, the cord develops a new activity, if the lesion has not altogether destroyed its functions. The manifestations of this new activity, the so-called "defensive reflexes," form the subject of the second half of this work. He deals in detail with the "triple flexion" reflex, direct reflex extension of the whole limb and the homolateral flexion with contralateral extension evoked by violently bending the great toe downwards. The discussion is accompanied by graphic records of the movements described, taken in cases of spastic paralysis. He accepts the view that the extensor plantar reflex is a part of complete limb flexion, but as

he attributes all these reflexes to forms of "stepping" and denies their defensive origin it follows that the Babinski extension of the great toe is also part of the act of walking. This position is opposed to the view held by Sherrington and his followers.

An Anatomical Guide to Experimental Researches on the Cat's Brain : A series of 35 frontal sections. By Dr. C. WINKLER, Professor of the Municipal University in Amsterdam, and Dr. ADA POTTER. Pp. 133. Amsterdam : Versluys, 1914.

The cat's brain was cut into frontal sections and thirty-five positions have been chosen for illustration. Each plate is accompanied by a complete description and occasionally by accessory figures illustrating special points, as, for instance, the microscopical structure of the cortex cerebri. The object of this work was to provide a descriptive basis for experimentation on the cat's brain, but the plates are so clear and so excellently reproduced that they are in themselves of permanent interest. The generosity of Mr. Laan has not only made it possible to produce this atlas, but has enabled the authorities of the neurological laboratory in Amsterdam to offer it to those institutions engaged in serious neurological work.

Die Halluzinosen der Syphilitiker. Von Privatdozent Dr. FELIX PLAUT. S. 116. Berlin : Springer, 1913.

This forms one of the monographs edited by Alzheimer and Lewandowsky, and is of great interest, firstly, as the latest opinion of Plaut on the condition of the cerebrospinal fluid in various forms of syphilitic affections, and secondly as the record of an ill-understood group of syphilitic manifestations. He believes that the Wassermann reaction is positive in the cerebrospinal fluid from most patients with syphilis, although "a metaluetic process is out of the question." The absence of a positive reaction in the blood gives an 80 per cent. probability against cerebrospinal syphilis. The author then describes at considerable length a number of cases of syphilis of the nervous system which simulated dementia præcox, primary dementia, hallucinatory paranoia and other forms of mental disease. Particular stress is laid on cases where hallucinations were present.

Meningococcus Meningitis. By HENRY HEIMAN, M.D., and SAMUEL FELDSTEIN, M.D. With introduction by HENRY KOPLIK, M.D., all of Mount Sinai Hospital, New York. Pp. 313, with 4 Plates and 31 Figures. Philadelphia : Lippincott, 1913.

This little book is by far the best account we have seen of cerebrospinal meningitis due to the *Meningococcus intracellularis*. Each chapter deals with one aspect of the disease in a succinct, accurate, and at the same time eminently

readable fashion. The history, bacteriology, epidemiology, mode of dissemination, pathological anatomy, and clinical types of the disease are excellently described. Infantile postbasal meningitis is shown to be due to the same cause as the epidemic forms; the condition of the cerebrospinal fluid and the best methods for lumbar puncture and serum infusion into the spinal canal are clearly laid down. The mode of action and composition of the four sera, most commonly employed, are stated, and the clinical results put forward without exaggeration. The chapter on treatment is evidently the fruit of much personal experience.

Beiträge zur Frage nach der Beziehung zwischen klinischem Verlauf und anatomischem Befund bei Nerven- und Geisteskrankheiten.
Bearbeitet und herausgegeben von FRANZ NISSL, in Heidelberg.
Erster Band, Heft 1. S. 91, mit 34 Figuren. Berlin: Springer, 1913.

Professor Nissl came to the conclusion that there was not sufficient intellectual co-operation between the clinician and the pathologist; each was interested in his own aspect of the case, and neither was competent to appreciate the other's point of view. The pathologist was not capable of carrying out the clinical examination of a patient up to modern requirements, and so lost touch with the clinician, who was equally unable to make a complete histological examination. He therefore selected certain cases, not necessarily rare or peculiar, for complete study by a clinician and a pathologist. Meetings were held at which these results were brought before all the assistants and other workers in the clinic; at the same time the specimens were shown and explained. These combined reports were so successful that he determined to publish them, and this pamphlet, containing a description of three patients, is the first part of vol. i. The first is a case of syphilitic mesaortitis and endarteritis obliterans of the cerebral vessels; the pathological report is excellent, but its interest is greatly enhanced by the complete life-history of this old soldier, work shy, alcoholic, violent and given to petty thieving. The second case is an atypical one of dementia paralytica, and the third a combination of this disease with arterio-sclerosis and gummatous cerebral syphilis. These are just the "common" cases which excite little interest without the close co-operation of the clinician and the pathologist.

Trauma und Nervenkrankheiten. Von PAUL SCHUSTER, in Berlin
[Sonderabdruck aus dem Handbuch der Neurologie von
LEWANDOWSKY]. S. 128. Berlin: Springer, 1913.

This is a reprint of Dr. Schuster's article in Lewandowsky's Handbook. He points out that the whole aspect of the medical man towards an injury has changed since the introduction of Workmen's Compensation, and the theme of this article is the effect of an accidental injury on a diseased and on a

presumably normal nervous system. He deals with the questions of long deferred apoplexy, the possible traumatic origin of general paralysis, tabes dorsalis, syringomyelia, myelopathies and other forms of organic diseases, and then gives a short account of traumatic hysteria and the neuroses. The article is extremely practical and should be consulted by anyone who expects to be cross-examined on these difficult aspects of injury to the nervous system.

Die Hysterie. Von Professor Dr. M. LEWANDOWSKY, in Berlin [Sonderabdruck aus dem Handbuch der Neurologie von LEWANDOWSKY]. S. 192. Berlin: Springer, 1914.

Like most of the chapters in the Handbook this article is a full and judicial summary of the present state of our knowledge on hysteria. It is clearly arranged, has an excellent index, and is written in an easy and attractive style. The list of authorities at the close is well selected and contains all the important papers.

Les Techniques anatomo-pathologiques du Système nerveux. Par GUSTAVE ROUSSY et JEAN LHERMITTE. Pp. 255. Paris: Masson, 1914.

This is an excellent manual of histological methods applicable to the nervous system. It is clear, practical, and every procedure recommended seems to have been tested by personal experience. The chapters follow the natural order of preparation of tissues, hardening fluids, section cutting and embedding; staining of the cell of the myelin sheath, of the neuroglia, and of the vascular and connective tissues are considered in separate chapters. The various methods for revealing products of degeneration are given in full, and the last three chapters are devoted to the peripheral nerves, the muscles, and the staining of bacteria.

Anatomia Clinica dei Centri Nervosi. By Professor G. MINGAZZINI. Pp. 936. Turin: Unione Tipografico-editrice, 1913.

An admirable text-book of anatomy of the central nervous system directed particularly to elucidate clinical conditions. The figures are clear and well reproduced, and the descriptions excellent. Such conditions as aphasia are illustrated by the lesions discovered in actual cases familiar from the literature of the subject, and everywhere accurate references are given for the views expressed and examples given.

B R A I N .

PARTS III. and IV., VOL. 37.

DISTORTIONS OF THE VISUAL FIELDS IN CASES OF BRAIN TUMOUR.

(*Fourth Paper.*)

CHIASMAL LESIONS, WITH ESPECIAL REFERENCE TO BITEMPORAL HEMIANOPSIA.

BY HARVEY CUSHING, M.D., AND CLIFFORD B. WALKER, M.D.

From the Peter Bent Brigham Hospital, Boston, Mass., U.S.A.

INTRODUCTION : SOURCE OF MATERIAL.

THE preceding papers in this series were devoted (1) to a statistical review of the perimetric studies in a series of 200 cases of brain tumour observed at the Johns Hopkins Hospital between June 18, 1905, and January 1, 1911 [7]; (2) to the deviations, particularly of the colour fields, in relation to the advancing stages of choked disc in the same series of cases¹ [8]; and (3) to the question of binasal hemianopsia and the tendency of this deviation to characterize the last stages of a declining choked disc [9].

In the first paper of the series it was stated that the use of the perimeter was possible in 123 of the 200 consecutive cases on which our statistical studies were based, and that in six of these cases a more or less typical bitemporal defect was found. Thus in 3 per cent. of the entire early series, or 4·9 per cent. of the cases in which perimetry could be used, the distortion of the fields indicated a median involvement of the chiasm. These figures, therefore, represent the average occurrence of bitemporal hemianopsia in the general run of brain tumour cases, for up to January, 1911, the number of hypophysial growths in the tumour series was not disproportionate, as it has since become. Thus in the 130 additional patients with brain tumour

¹ This question of colour interlacing, upon which we place less importance than formerly, will be further reported upon by one of the present authors (Walker).

observed in Baltimore between January 1, 1911, and May 1, 1912, the number of pituitary cases so far increased as to greatly alter what might be considered the average percentage figures; and this disproportion has been even more marked in the Boston series of 134 cases at the present writing, July 1, 1914.

In the analysis of our "brain tumour" cases, we were from the first led to include a number of patients with hypophysial or infundibular growths—growths which, though intracranial in a strict sense, represent purely extracerebral lesions, distorting the brain proper either not at all or very late in their progress. The number thus included, however, does not represent all the examples of hypophysial disease in the series, for only 101 of the 148 cases observed up to July 1, 1914, deserve, on the basis of neighbourhood pressure symptoms, to be classified among the intracranial tumours, and in only 81 of these were the fields of vision affected. The remaining cases comprise acromegalics and others who have thus far at least failed to show clinical signs of involvement of the chiasm.¹

From the foregoing it can be seen, in the first place, that perimetric distortions are wanting in nearly half of the examples of hypophysial disease in the stage at which they are commonly recognized to-day;² and in the second place, that in about 20 per cent. of the patients actually showing characteristic neighbourhood symptoms there occurs no perimetric change demonstrable by our present methods. It may be gathered, therefore, that the chiasmal "cross-roads" are capable of considerable distortion by a growth in the interpeduncular space without a demonstrable encroachment upon the fields of vision. This, moreover,

¹ In every patient suffering from a pituitary disorder, as has been elsewhere emphasized by one of us ("The Clinical Aspects of Dyspituitarism," The Harvey Lecture, December 10, 1910), there are three separate clinical factors to be distinguished: (1) The *neighbourhood signs and symptoms*, shown by evidences of pressure on adjoining structures—chiasm, oculomotor and olfactory nerves, uncinate gyri, crura cerebri, and the like—and often by a demonstrably enlarged sella turcica; (2) the *general pressure symptoms* in case the growth actually becomes large enough to cause considerable cerebral deformation or to obstruct the cerebrospinal fluid circulation by blocking the foramina of Munro; and (3) the *constitutional or glandular symptoms*, either on the side of over- or under-hypophysial activity.

The first and second of these factors alone are of interest in connection with perimetry, for one of the most striking of the neighbourhood signs—indicating chiasmal pressure—is represented by a supposedly characteristic distortion of the visual fields associated with so-called primary optic atrophy. In some cases, however, a choked disc may become superimposed on the primary nerve lesion, with changes due to a so-called secondary atrophy, which may modify the perimetric outlines according to the principles set forth in the earlier papers.

² Doubtless these figures will fall markedly as more precocious diagnoses are made, based on constitutional disturbances rather than on neighbourhood symptoms.

has been demonstrated in a few cases in which supposedly normal fields were plotted shortly before death, and yet in which an extraordinary degree of deformation and elongation of the chiasm was disclosed *post mortem*. And what is of still greater moment, a *bitemporal* hemianopsia, or a tendency in this direction, is by no means the necessary expression of the chiasmal involvement when vision does become affected by a hypophysial lesion, for nearly half as many cases in the series have shown an equally definite *homonymous* hemianopsia or a tendency in that direction. In its so-called typical form furthermore, with a practically vertical meridian which sharply divides in each eye the blind nasal from the seeing temporal retina, a *bitemporal* hemianopsia is far from the most common form of field defect. Hence the conclusion that an existent clean-cut bitemporal hemianopsia is an evidence of a medial lesion, most often due to a tumefaction of the hypophysis or its stalk, is justifiable enough; but the reverse argument does not hold—that the absence of this characteristic defect, or indeed of any defect whatsoever in the fields, necessarily speaks against a primary pituitary or interpeduncular growth.

Though it will be fully emphasized that the important feature of these field deformations due to chiasmal lesions is their progressive nature, nevertheless it may be well to give some figures in regard to their relative frequency, and possibly the best fixed point is the time of the patient's hospital admission, representing at the present day, unhappily, a fairly well advanced stage. For our present purposes these patients may be divided into four main groups: (1) those with a bi-temporal defect of vision; (2) those with a homonymous defect; (3) those already blind in one or both eyes, under which circumstances it is often difficult and sometimes impossible to tell in which group—bitemporal or homonymous—the case actually belongs; and (4) the cases with irregular defects, which are scarcely to be classified. In these four groups the 81 examples in our series fall as follows:—

(1) *The bitemporal group*.—Here are included 26 patients, of whom 7 showed acromegalic changes, the other 19 being examples of primary hypophysial insufficiency. In four patients a characteristic bilateral temporal hemianopsia was present with fairly vertical meridian, though in only one instance was the degree of macular involvement practically equal in the two eyes. In nine cases there were fairly symmetrical defects in the temporal fields, but the stage of a vertical meridian was not yet reached or had been passed by. In another nine patients a tendency towards a bitemporal field constriction was evident, but the field defects

were very asymmetrical on the two sides. It may be added that in several cases (necessarily excluded from these statistics) the fields on the first admission were normal but on subsequent examinations the early grades of an advancing temporal constriction began to appear.

(2) *The homonymous group*.—Of the twelve cases included here, four being acromegalics, the defect in three was typical, with a vertical meridian separating the blind from the seeing retinae. In four cases there was a symmetrical defect in a stage short of the vertical hemianopsia, and in the remaining four an unmistakable homonymous defect was evident, though the process was very unequal in the two eyes. In two of them normal vision in one eye was associated with a nasal defect in the other—an early stage of what ultimately became a homonymous defect.

(3) *The amaurotic group*.—This group comprises 35 patients, only three of them acromegalics, who on admission were blind in one or both eyes. (a) There were four who according to the history, or from *post-mortem* findings, were shown to belong in the group of bitemporal cases. In one instance there was a homonymous return of vision after operation, and it is uncertain in which group the remaining six belong. (b) There were 24 patients totally blind in one eye and showing on the other side either a practically normal field (three cases), or a typical temporal hemianopsia (seven cases), a tendency towards a nasal defect (one case), or an atypical field distortion, making it difficult to tell whether the case belonged in the homonymous or bitemporal group (three cases). The same uncertainty on admission pertained to the 17 cases showing a temporal defect which might have been associated originally either with a primary nasal or a temporal blindness in the other eye, but in nine cases, either by the history or by post-operative return of vision, the condition was shown to have been bitemporal.

(4) *The unclassified group*.—Here are included eight cases in which bizarre fields accompanied known pituitary lesions. They comprise cases with central scotomas associated with normal or more or less normal peripheries, one case with a fairly sharp superior hemianopsia, and others with more or less irregular outlines of indeterminate nature, some of them representing our early experiences with perimetry which leave some doubt as to the exactness of the plotted records.

These figures, be it recalled, refer merely to the findings on admission, and before we became familiar with the early gradations of the process in but few of the cases would we have ventured, on the basis of the perimetric studies alone, to predict the presence of a retrochiasmal

lesion. As will be pointed out, the characteristic features of the chiasmal implication in these patients is the progressive involvement of the fields for colour as well as those for form and the associated alterations in central vision (acuity and scotomata). We hope to show what are the earlier perimetric indications of the chiasmal lesion, for the tyro knows the significance of a bitemporal hemianopsia at the stage when a vertical meridian divides blind from seeing field.

Though it was our original intent to include in this report all the cases showing field defects with primary atrophy due to a direct involvement of the chiasm by a hypophysial, or interpeduncular tumour, we have thought it best to reserve the cases with homonymous hemianopsia due to pressure of a tumour against the side of the chiasm for a separate report, since, owing to their presumed rarity—only a few examples are on record—they deserve special emphasis. The present paper, therefore, concerns itself with the cases exhibiting obvious bitemporal defects, together with those in the amaurotic group, which in all likelihood belong also in this category.

BITEMPORAL HEMIANOPIAS IN GENERAL.

Incidence.—Though first noted by Mackenzie in 1835, and known to von Graefe in 1856, surprisingly few cases of bitemporal hemianopsia were recorded until the present interest in hypophysial disorders was awakened. In 1880 43 examples were gathered by Wilbrand, some of doubtful chiasmal origin. Griffith, six years later, added 15 cases, four in his own experience; and Seli in 1894 brought the recorded number up to 70, but even at that time very little emphasis was laid on hypophysial lesions as a causal agency. In an elaborate statistical study in 1912 [5] Bogatsch added 34 cases from Uhthoff's clinic in Breslau, and stated that he had record of 315 cases in the literature. In illustration of the growth of our knowledge of pituitary disorders it may be added that according to Bogatsch, of the 59 cases reported before 1886, the date of Marie's description of acromegaly, only 5 per cent. were accredited to hypophysial lesions, whereas in 40 per cent. the cause was said to be unknown, and that in the 256 cases reported subsequently 50 per cent. were ascribed to the hypophysis and only 13 were of unknown etiology. With but few exceptions, in our series the hypophysis or a lesion in its neighbourhood associated with or affecting the hypophysis, such as the interpeduncular tumours which arise on a congenital (pituitary) basis, has been the causal factor.

In the experience of various writers bitemporal hemianopsia occurs in the proportion of 1 to 25 in all cases of hemianopsia, including, of course, the frequent examples due to cerebral vascular lesions. In our statistics, confined to the hemianopsias associated with intracranial tumours, there were 80 examples (including 17 so-called binasal hemianopsias) in the 330 cases observed between June 18, 1905, and May 1, 1912. In these 80 examples there occurred 23 of bitemporal involvement—a proportion of about 1 to 3. This high percentage of bitemporal hemianopsias—which would be even greater did the computation include the Boston cases—is attributable not only to the fact that the series comprises an unusual number of hypophysial cases, and includes moreover, as “bitemporal,” cases showing a tendency only toward this defect, but also to the fact that the cerebral vascular lesions, doubtless the most common source of homonymous hemianopsia, naturally are not represented in the series except as an occasional case with a pseudo-tumour syndrome.

Mode of production.—Despite some difference of opinion in regard to the results of various experimental observations on the degree of completeness of the chiasmal crossing in higher animals,¹ the painstaking observations of Henschen [15] on carefully selected clinical material furnish the basis for the most generally accepted ideas in regard to the disposition of fibres in tract, chiasm and optic nerves. Though Henschen's figures, modified slightly by Wilbrand and Saenger, are familiar enough to ophthalmologist and neurologist, nevertheless for the purpose of reference we have ventured to insert new diagrams in this context (fig. 1) as an aid in the interpretation of what is to follow.

As de Schweinitz and Carpenter have pointed out [11], there are probably many individual human variations, all the way from an entire absence of crossing (of which we have seen one example in association with a congenital suprasellar cyst) to a possible total decussation, representing a reversion to the lower and more primitive type of chiasma. In the macular bundle, in particular, variations may occur, some even believing that it has a bilateral cortical representation, and as the question of inclusion or sparing of the macula has been thought to be of considerable importance from a localizing standpoint it is well to have the anatomical relations of the various bundles clearly in mind.

There are three pairs of fibre-bundles or fasciculi to be considered, the uncrossed, the crossed, and the central or macular bundles.

¹ The question is thoroughly reviewed by L. F. Barker [1].

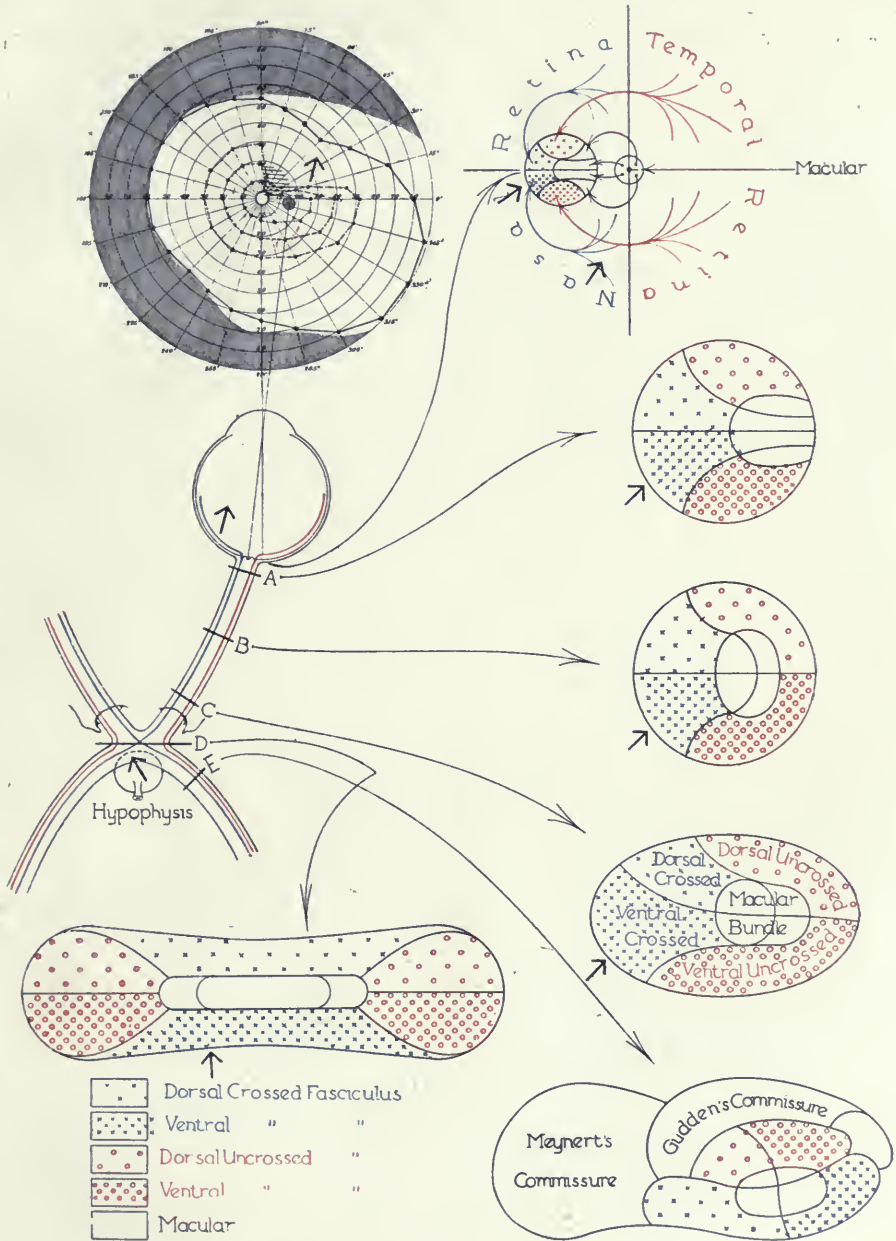


FIG. 1.—Diagram based on Henschen's conception of the disposition in the optic nerve of the several fasciculi. There is indicated an hypothetical involvement of the ventral crossed fasciculus from the right eye, which has produced Stage I. of a right temporal defect (*cf.* perimetric field). The path of the fibres between the point of pressure at the chiasm and the retina is indicated by the short arrows.

The uncrossed bundles (*fasciculi non cruciati*) arise in each eye from the temporal half of the retina, and for the most part retain a lateral position in optic nerve, chiasm and tract as far as the geniculate bodies. In this position they naturally are best protected from the effect of a mesially placed (e.g., retrochiasmal) lesion. Each uncrossed bundle is made up of a dorsal and ventral portion arising from the dorsal and ventral quadrant of the corresponding temporal retina. A bilateral injury of these bundles may, as pointed out in our last paper, give a binasal hemianopsia; a unilateral injury involving one bundle alone, a nasal hemianopsia of the corresponding eye; injury of the ventral fibres alone, an upper quadrantal loss of nasal vision, and so on.

The crossed bundles (*fasciculi cruciati*), likewise composed of dorsal and ventral fibres, arise from the nasal half of each retina, enter the inner (nasal) side of the papilla, pass down the mesial side of the optic nerve, cross at the chiasm and continue down the ventral side of the opposite tract to the contralateral geniculate bodies. These fibres therefore are the most exposed to the effect of a mesially placed lesion, and consequently are the ones most often implicated by hypophysial growths with the resultant bitemporal blindness. Moreover, as the ventral fibres which arise from the lower nasal quadrants remain ventrally disposed throughout their course, when the chiasm is primarily affected by pressure from below, as it is likely to be in the case of a hypophysial tumour, the defect should appear first of all in the upper temporal fields, as illustrated in the diagram. If, on the other hand, the growth is likewise mesial but of infundibular rather than hypophysial origin, the dorsal fibres of the crossed bundle arising from the upper nasal retinal quadrant would be expected to suffer first, with the primary defect showing in the lower temporal quadrant of the field of vision. This, however, is a comparatively rare condition.

The macular fibres (*fasciculus macularis*) leave the retina from the region of central vision about the fovea and enter the temporal side of the optic papilla, separating the dorsal and ventral fibres of the uncrossed fasciculus as they approach the papilla from the temporal retina. From its lateral position as it enters the optic papilla the macular bundle gradually assumes a more central position as it passes down the nerve, where it becomes covered in by the uncrossed fasciculus; though, as a matter of fact, it actually remains somewhat eccentric. It consists, furthermore, of a crossed and uncrossed division—the latter lying in juxtaposition to the uncrossed fasciculus proper, the former crossing at the chiasm together with the crossed fasciculus proper from the nasal retina.

As the macular bundle occupies a somewhat protected position throughout its course, one might conjecture that as a consequence of pressure against nerve, chiasm or tract it would suffer later than the crossed fasciculus in the case of medial pressure and later than the uncrossed fasciculus in the case of lateral pressure. It would appear, however, that the macular fibres are especially vulnerable and, when affected as a consequence of pressure, are

less capable of complete restoration than are the more peripherally disposed fibres.¹

Types of bitemporal distortion.—Nine possible types or combinations of bitemporal defect, with illustrative cases from the literature, were enumerated some years ago (1897) by Wilbrand in his excellent chapter on "Perimetry and its Clinical Value" in Norris and Oliver's "System of Diseases of the Eye." They were as follows²:—

(1) Typical temporal hemianopsia in one eye; in the other the upper and outer quadrant being lost.

(2) Typical temporal hemianopsia in one eye; in the other the lower and outer quadrant being lost.

(3) Only the upper and outer quadrant lost in each eye.

(4) Only the lower and outer quadrant lost in each eye.

(5) Complete blindness in one eye, with temporal blindness in the other.

(6) Complete blindness in one eye, with upper nasal quadrant remaining active in the other.

(7) Complete blindness in one eye with lower nasal quadrant remaining active in the other.

(8) The upper nasal quadrants of both eyes alone remaining active.

(9) The lower nasal quadrants of both eyes alone remaining active. (No reported case.)

In the writers' series, illustrations occur of practically all of these types, and it would be possible, indeed, to add a great number of other combinations to those which Wilbrand has given, particularly if the various hemianopic or quadrantal colour distortions and the sparing or otherwise of the macula in the form or colour field outlines be regarded as types. One might include such field deformations as the following:

(1) The sector defects which occur primarily in the colour fields, more often appearing first in the upper temporal quadrants; (2) blindness in one eye with (a) a normal field in the other, or (b) involvement of only a single quadrant of the nasal retina of the other, or (c) with so inconspicuous an upper temporal field defect that it may easily escape detection, or (d) a lower temporal field defect of equally slight grade;

¹In the last paper of this series when we come to discuss the lesions of the geniculocalcarine pathway it will be pointed out that these divisions into dorsal and ventral bundles for crossed and uncrossed tracts still hold in a measure for the cerebral relay of the visual pathway. That this is particularly true of the temporal loop of this pathway has been clearly shown by Adolph Meyer.

The question of sparing or otherwise of the macula in central versus peripheral lesions must likewise be deferred to a later paper.

²Lest there be some confusion it may be said that throughout this paper when we speak of a nasal or temporal hemianopsia we refer to that half of the visual field and not to the retina itself.

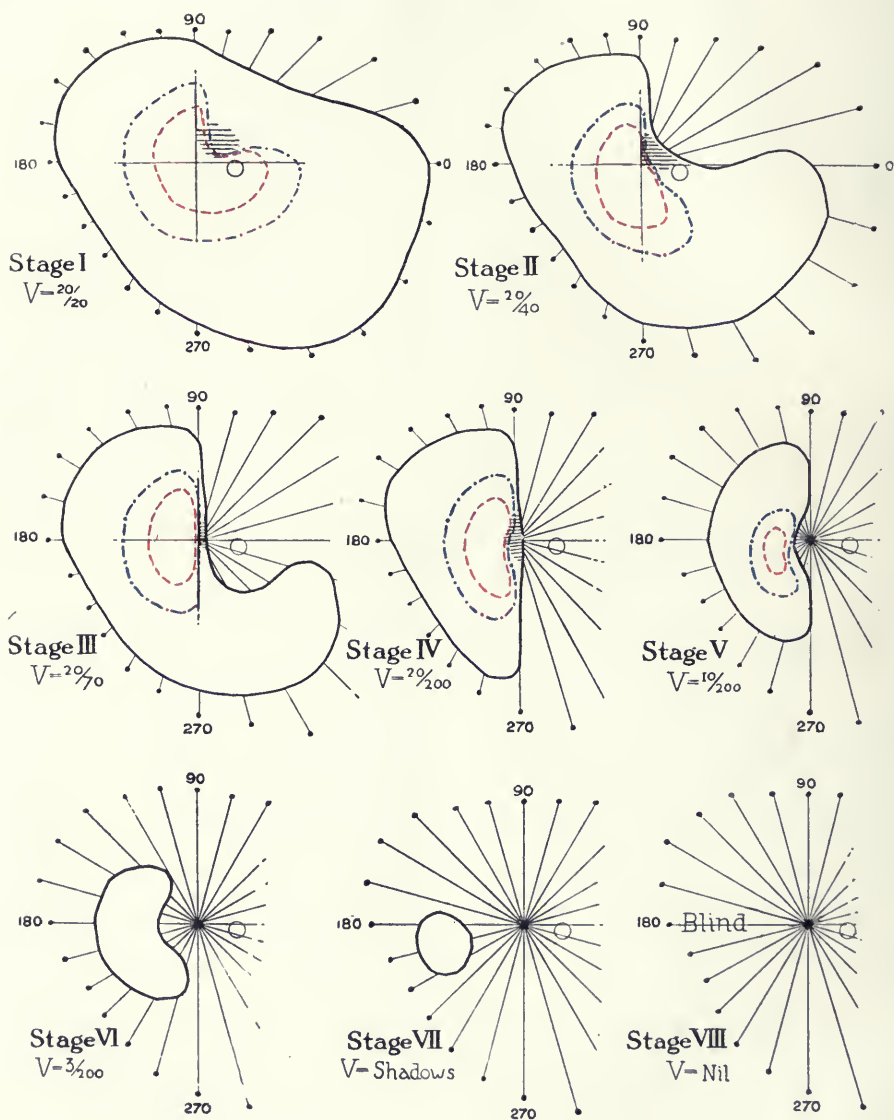


FIG. 2.—Showing the eight stages of a progressing right temporal defect.

(3) blindness in one eye with superior hemianopsia in the other, the ventral crossed and uncrossed fasciculi being completely blocked, whereas the dorsal fibres are largely spared. Thus, were classifications of this sort worth recording, an infinite number of types of increasing complexity might be given. Wilbrand himself states that "the fields of vision found in diseases of the chiasm afford only a glance, as it were, into the momentary condition of the path."

Hence it seems to us far more preferable to look upon the perimetric deviations as stages rather than types, particularly as the condition in the two eyes rarely progresses symmetrically, and we have consequently arranged the cases from this viewpoint.

STAGES OF TEMPORAL HEMIANOPSIA.

The periods in an advancing process which we have come to speak of as "stages" we have enumerated serially, from the normal field to the stage of blindness. These steps, or stages, have been selected out of the many possible ones for the reason that the larger number of our cases happen to have been caught in them, and not with the idea that the advancing process tends to halt at these separate stages, except possibly in Stage IV. In the following description of these stages (cf. fig. 2) the average measurement of vision estimated from the tests on eyes which in our perimetric records accord with the stage in question, is also given.

Stage I shows merely an upper temporal quadrantal defect in the colour fields, often with a slight slanting off of the form fields in the same quadrant. At this time a paracentral relative or absolute scotoma not infrequently may also be made out in the upper temporal quadrant. In this stage the patient usually has central vision of $\frac{2}{20}$, but may be conscious of a slight central haziness which, however, is difficult of objective demonstration with ordinary methods of perimetry.

Stage II.—The defect in the upper temporal quadrant, anticipated by the slant in the form field of Stage I, becomes realized and the colour fields recede considerably in the lower temporal quadrant. The paracentral scotoma persists in whatever may be left of the quadrant, and in patients with good powers of observation the limits of a relative central scotoma may occasionally be outlined. Central vision falls to an average of $\frac{2}{40}$.

Stage III.—Here complete temporal hemiachromatopsia is usually present for smaller discs, but for larger sized discs colour vision can often still be demonstrated across the mid-line in the lower quadrant. In passing into this stage it is notable that the temporal form field sinks below the horizontal line, particularly in the region of the blind spot, after the manner of an enlargement.

There is also a peripheral contraction, so that the resulting outline is variably gourd-shaped.

The relative central scotoma is present, and a hemiopic pupillary reaction is usually demonstrable by the rotary shutter test. Central vision becomes $\frac{2}{50}$ to $\frac{2}{70}$.

Stage IV.—Hemianopsia has become complete for form and colour, the macula often being spared by the otherwise vertical meridian.

The relative central scotoma increases in size for form and becomes absolute for colour, green usually being lost before red and red before blue. Vision stands at $\frac{2}{70}$ to $\frac{2}{100}$.

Stage V.—At this stage there is definite constriction of the remaining hemianopic colour and form fields, and the latter may begin to show constriction either above or below, but more often below.

The relative central scotoma becomes absolute, and eccentric vision is about $\frac{1}{100}$.

Stage VI.—Colour vision is lost except occasionally for large discs. The nasal form field begins to shrink away from the vertical meridian.

Central vision is nil, and eccentric vision reduced to the neighbourhood of $\frac{5}{100}$.

Stage VII.—A small area is left in the nasal field, which can be barely outlined with large discs or with small flash-lights. Vision is reduced to shadows or light perception.

Stage VIII.—Blindness. Pupillary reactions nil.

The least affected eye in the meantime is progressing along the same route, for it cannot be too strongly emphasized that the process rarely advances with equal steps in the two eyes. Thus we may see Stage VIII—namely, of blindness—in one eye when the other has not passed beyond Stage I or Stage II, or has retrogressed to Stage II or Stage I, or indeed may have become normal. It is important to appreciate, moreover, that there are probably recessions and advances in the process from time to time, though the general tendency of the condition, unoperated, is toward an advance. It is quite possible that in this way the macular fibres may become involved, and also that they are somewhat more vulnerable than the other fibres, so that after an advance up to the point at which the macular bundle is involved, even though there is a recession in the process with widening of the fields, a relative scotoma of the fibres of the macular bundle may be left in the involved quadrant (cf. Case 3). This may possibly account for the presence of these scotomas, which Bartels, in Germany, and de Schweinitz and Halloway [12] in this country were the first to describe in detail, and we have been able to corroborate their findings in a great number of our cases. Another explanation has been offered by

J. Herbert Fisher [13], who suggests that the process is the result of traction upon, rather than of pressure against, the chiasm, and that the macular fibres, owing to their highly specialized function, may suffer more than the others. It would seem to us that the two conditions, pressure and traction, must go hand in hand; and as a matter of fact we have come to believe from our *post-mortem* studies that in most cases the tracts suffer far more than the optic nerves or chiasm, for they may be thinned out by pressure into mere ribbons even when the chiasm shows relatively little deformation.

It is quite apparent that in the majority of these cases the upper fields suffer more than the lower,¹ and this is apt to be so even in the advanced stages, for there are a number of examples in the series in which merely a small patch of vision remained in the lower nasal fields, where shadows of large discs were still perceived. Moreover in one or two cases a small patch of vision has returned after operation in the lower nasal quadrant of a previously blind eye (cf. Case 6). In one case, too, there was a restoration of almost the entire lower field for form, suggesting a form of superior hemianopsia, the crossed and uncrossed dorsal fasciculi of the eye in question having escaped from complete destruction. Another interesting fact to which attention has already been called is that in the progressive constriction of the fields from Stage III to Stage IV—namely, from the gourd-shaped field to that of exact hemianopsia—a small point representing the tip of the gourd may remain isolated in the temporal field. Under these circumstances, with return of vision the field widens out from the lower zone and soon envelops this isolated patch (cf. Cases 5, 6 and 7).

The fact that the macular fibres may suffer most, as already suggested, is apparent also in cases in which after Stage IV has been reached and a successful operation has been performed, with subsequent widening of the fields to their normal peripheries, a relative central scotoma persists long after normal field peripheries have been regained (e.g., Case 3). When central vision is actually lost, in cases which have advanced beyond Stage IV, perimetric observations of any exactitude become impossible unless two points of eccentric fixation are employed.

Some of these stages can be well illustrated by giving a more or less complete series of charts from an individual history, for in some patients circumstances have permitted us to follow the condition over a long

¹ To this also J. Herbert Fisher [14] has called attention.

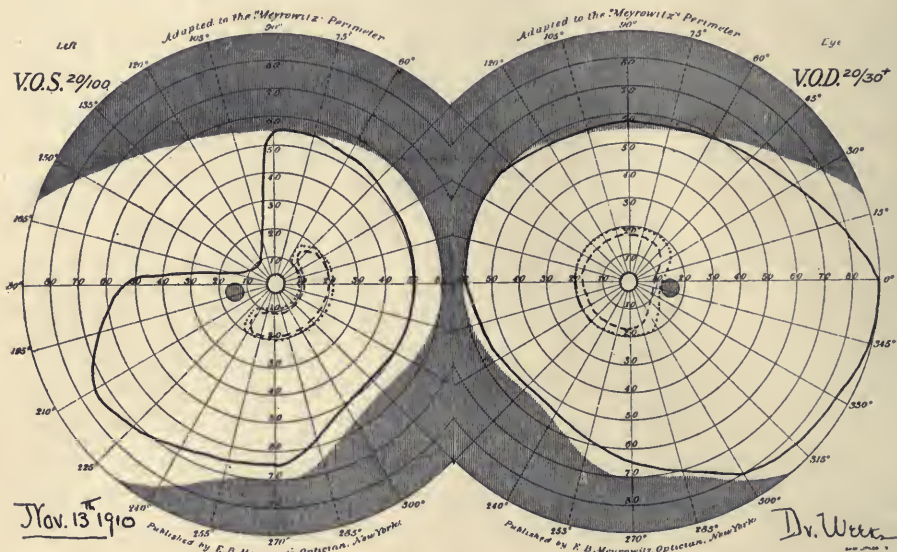


FIG. 3.—Case 1. Fields of November 13, 1910 (Dr. Weeks), fourteen months before operation. O.S., Stage II.

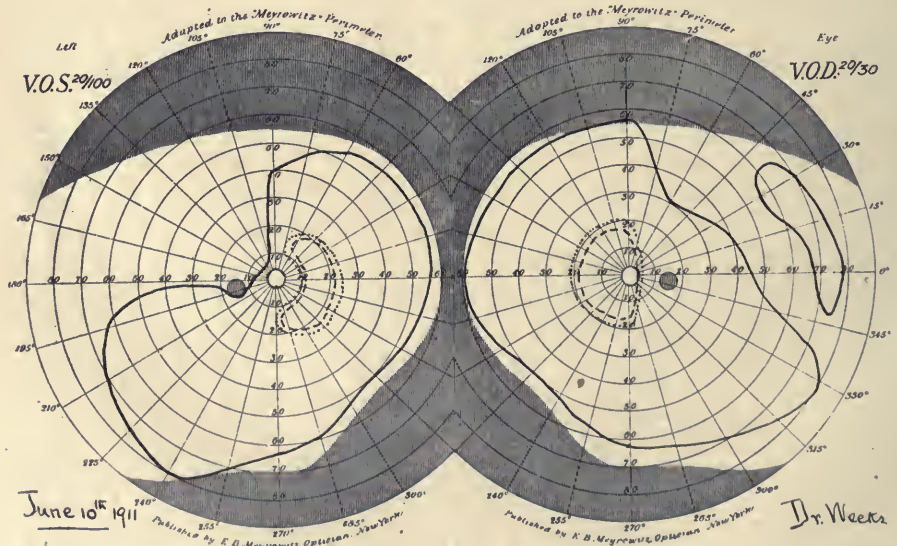


FIG. 4.—Case 1. Fields of June 10, 1911 (Dr. Weeks), seven months before operation. O.S., Stage II + ; O.D., Stage I.

period, so that we may have as many as twenty serial perimetric observations. In the following case, for example, our own charts were fortunately supplemented by observations taken elsewhere before the patient came under our care.

Case 1 (J. H. H., Surg. No. 29,117).—*Dyspituitarism, enlarged sella, bitemporal hemianopsia, operation, restoration of vision.*

January 20, 1912.—Admission of Miss E. V. H., aged 54; referred by Dr. John E. Weeks, of New York. Slight symptoms of dyspituitarism, with incipient acromegalic manifestations. The cranial X-ray shows a greatly distended sella. No headaches, nausea or vomiting; always strong and well.

Vision began to fail eighteen months ago. Four months later an opaque blur was observed in the upper left temporal quadrant; and gradually the entire lateral vision in the left eye was lost. Several months before admission a similar blur appeared in the upper right temporal quadrant, but this has not, as yet, advanced as far as on the left. Examinations by Dr. Weeks during this period verified these subjective symptoms (cf. figs. 3, 4, and 5, for November 13, 1910, June 10, 1911, and January 11, 1912). Vision decreased meanwhile to V.O.S. $\frac{20}{30}$, V.O.D. $\frac{20}{40}$. The process has been advancing with rapidity during the past few weeks.

Examination of eyes.—No diplopia, pupils equal and active to light, accommodation and consensually. Movements complete; no strabismus, nystagmus or von Graefe's sign. *Fundi*: O.D., optic disc shows a slightly heightened pallor of the nasal side, slight suggestion of arterio-sclerosis; otherwise fundus normal. Lamina cribrosa sharp. No swelling of disc. O.S. has the same appearance, with slightly greater pallor of the disc. Pupillary reaction roughly seems better from the nasal than from the temporal retinae. Wilbrand test negative. Pupillary reactions to the small lights of Hess (objectively with Krusius type of pupillometer) show no better response from the nasal than from the temporal retinae; patient could not use entopic method.¹ V.O.S. $\frac{10}{20}$, V.O.D. $\frac{20}{50}$.

Fields (fig. 6) show a bitemporal hemianopsia with the macula bisected on the right (Stage IV) and lost on the left (Stage V).

January 24.—*Fields* and acuity unaltered.

January 27.—*Transphenoidal operation.* Partial removal of struma. Perfect recovery, with subjective improvement in vision on the tenth day.

January 31.—*Fields* of this date show practically no change to small discs, and acuity remains unaltered.

February 9.—*Fields* show improvement; now almost typical bitemporal hemianopsia, the macular defect on the left being somewhat less extensive. V.O.S. $\frac{20}{30}$, V.O.D. $\frac{20}{40}$ —.

¹ Could this patient have been examined, as have been more recent ones, with a rotary shutter and strong illumination a hemiopic pupillary reaction would doubtless have been demonstrable. (*Tr. Ophth. Sect. Amer. Med. Assoc.*, June 1914, pp. 318-353.)

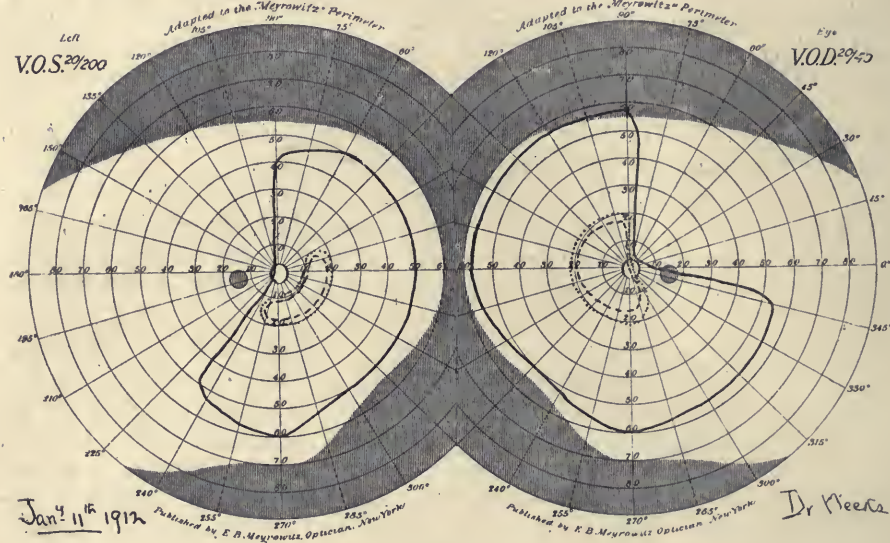


FIG. 5.—Case 1. Fields of January 11, 1912 (Dr. Weeks), sixteen days before operation.
O.S. Stage III + ; O.D. Stage II.

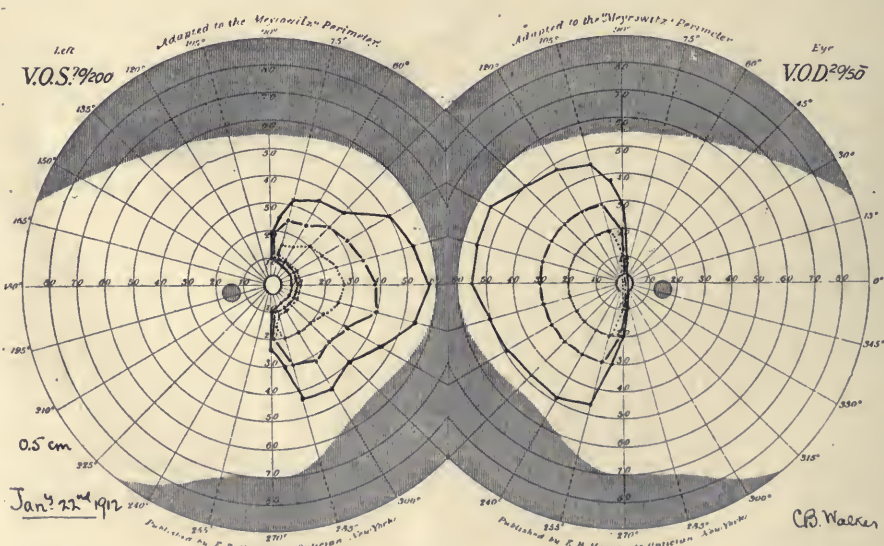


FIG. 6.—Case 1. Fields on admission, with 0.5 cm. discs, five days before operation.
O.S., Stage V ; O.D., Stage IV.

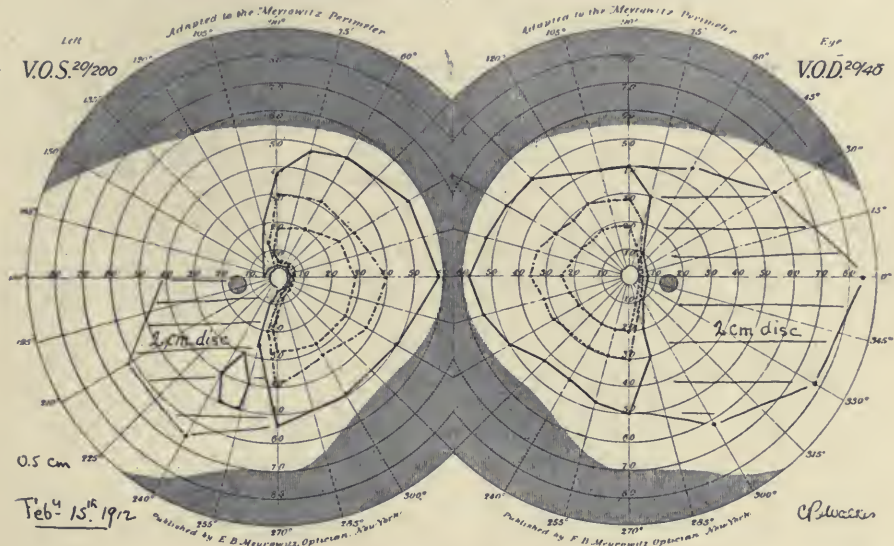


FIG. 7.—Case 1. Fields of February 15, 1912, nineteen days after operation, shaded areas to 2 cm. discs, showing marked recession.

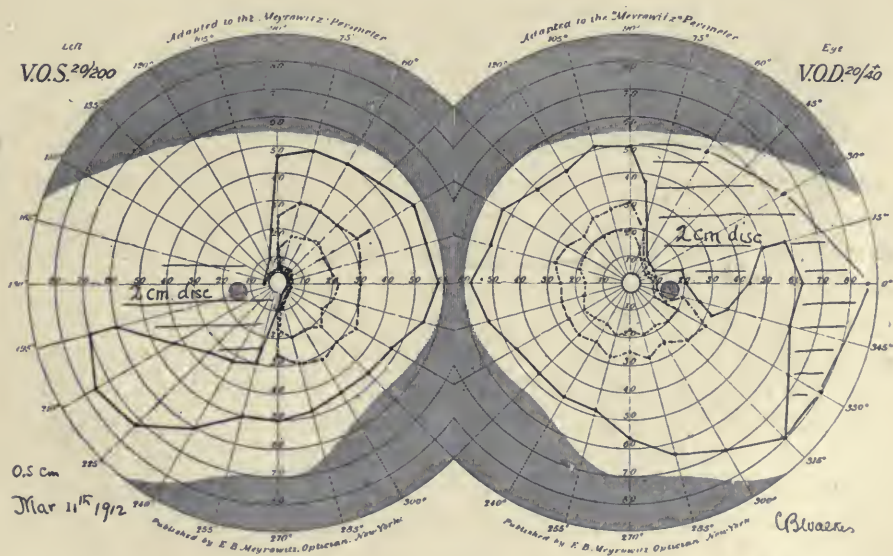


FIG. 8.—Case 1. Fields of March 11, 1912, six weeks after operation: shaded areas to 2 cm. discs. Showing recession O.S. to Stage III; O.D. to Stage II.

February 15.—*Fundi* unchanged. *Fields* (fig. 7) show marked improvement, with return of vision to 2 cm. discs in the whole right temporal field and lower left temporal field. V.O.S. $\frac{20}{200}$ —, V.O.D. $\frac{20}{40}$. Patient discharged.

March 11.—*Returns for observation*. *Fundi*: O.U. unchanged. *Fields* (fig. 8) show further improvement; recession on the right to about Stage II, and on the left to about Stage III. V.O.S. $\frac{20}{200}$, V.O.D. $\frac{20}{40}$.

April 5.—Report from Dr. Weeks. *Fields* (fig. 9) appear normal on the right; left in Stage II (?). V.O.S. $\frac{20}{200}$, V.O.D. $\frac{20}{20}+$.

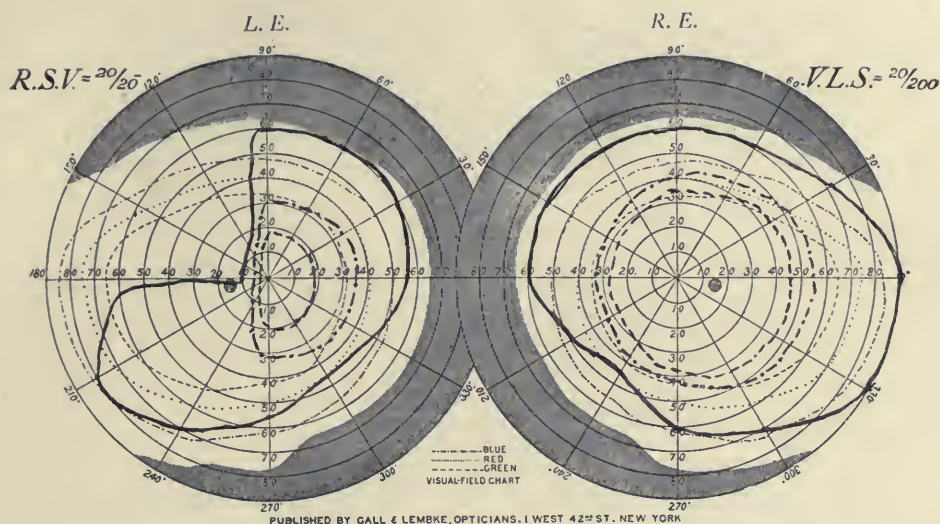
May 20.—*Returns for observation*. *Fundi*: O.D. normal except for very slight arterio-sclerosis and rather pale disc; O.S. disc paler than on the right but appearance otherwise the same. *Fields* (fig. 10) normal on the right and on the left approaching Stage II, with central scotoma. V.O.S. $\frac{20}{200}$, V.O.D. $\frac{20}{20}$.

July 22.—Reports by letter "almost perfect vision in both eyes."

September 18.—*Reports in person*. *Fields* (fig. 11), plotted for the first time with graduated discs, show more clearly than those of May 20 the character of the improvement on the left. V.O.S. $\frac{20}{200}$, V.O.D. $\frac{20}{20}$.

January 5, 1913.—*Reports in person*. *Fields* (fig. 12), the right remains normal and the left shows further improvement, but the central scotoma persists. V.O.S. $\frac{20}{100}$, V.O.D. $\frac{20}{15}$.

Comment.—This story illustrates in sufficiently typical fashion not only the manner in which the field defects usually advance, but also the manner in which recessions in the defects occur after the nerves have been relieved from pressure. It will be noted that the first charts taken by Dr. Weeks, on November 13, 1910 (fig. 3), showed our Stage II advancing to Stage III in the left eye, with an evident involvement of the ventral crossed fasciculus to that eye. It is quite probable that at that time more detailed tests would have shown a relative central scotoma, in view of the fact that the colour fields are so markedly constricted. The right eye at the same time was practically normal, or possibly in a latent condition of Stage I, for the evident constriction of the temporal colour fields shows that some change has occurred. Dr. Weeks's two subsequent charts (figs. 4 and 5) of seven and fourteen months later show a progressive advance in the left eye to Stage III and in the right to Stage II, and during the eleven days intervening between his last observation and the patient's admission there was a rapid advance to Stage V in the left and Stage IV in the right eye. After the operation there was a fairly prompt improvement on the right with return to normal from Stage IV in three months, and a slower but progressive return on the left from Stage V to Stage II during the year after the operation, which in all likelihood represents the high-water mark of possible restoration. As a matter of fact the



Dr. Weeks
April 5th 1912

FIG. 9.—Case 1. Fields of April 5, 1912 (Dr. Weeks), ten weeks after operation.

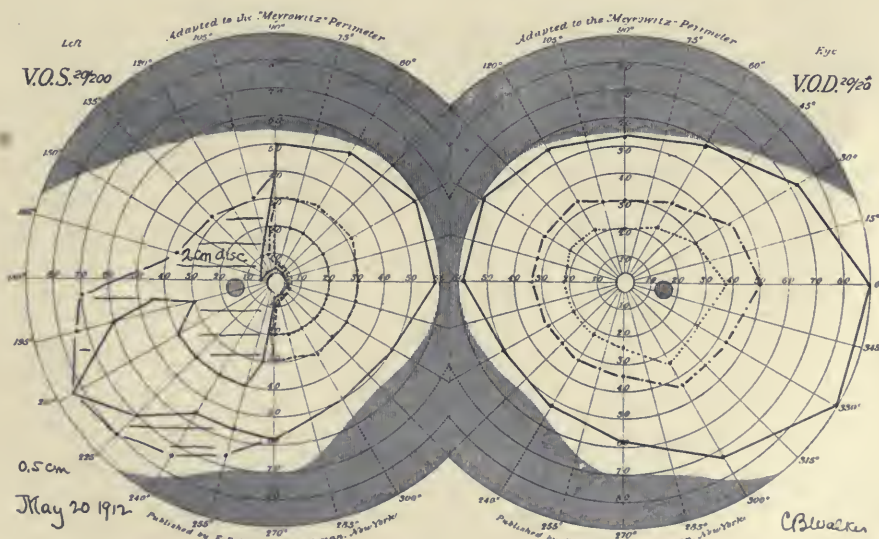


FIG. 10.—Case 1. Fields of May 20, 1912, sixteen weeks after operation; shaded area to 2 cm. disc. O.S. Stage III —; O.D., normal.

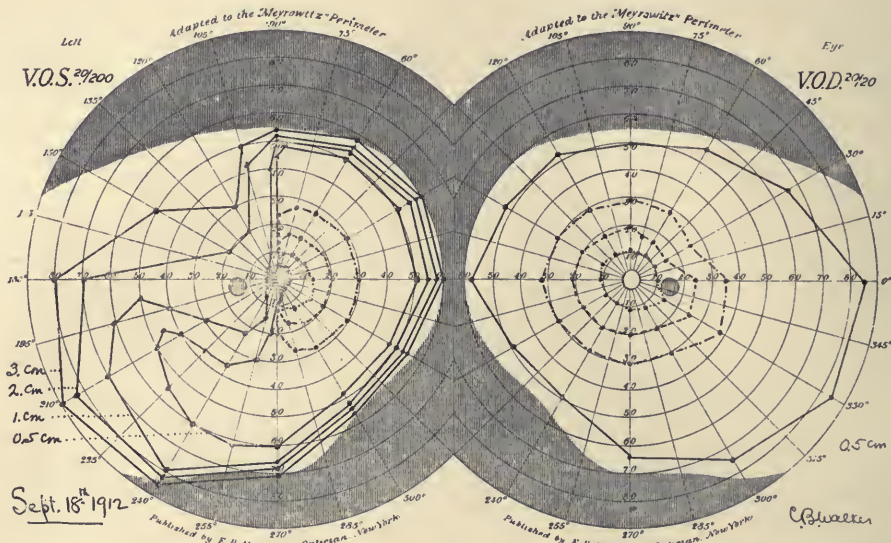


FIG. 11.—Case 1. Fields of September 18, 1912, by improved method with graded discs, eight months after operation. O.S., Stage III — ; O.D., normal.

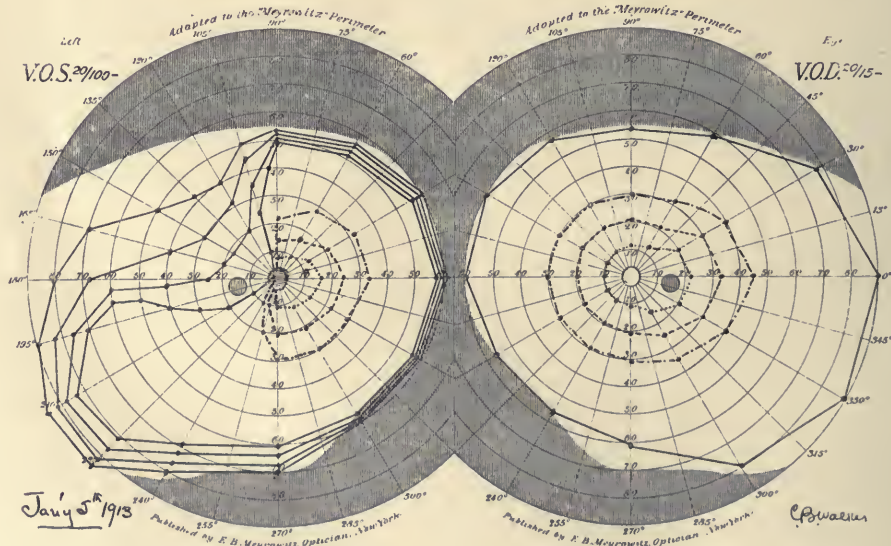


FIG. 12.—Case 1. Fields of January 5, 1913, one year after operation, showing further improvement. O.S., Stage II; O.D. remains normal.

improvement was much less rapid than is usually the case after a successful operation of this type when the process has not advanced beyond Stage IV. It is customary for us to see a much more striking restoration during the first few weeks, as will be apparent from some of the subsequent histories.

The case has been selected particularly for the reason that it illustrates the progressive improvement in the technique of making these observations, for in the fields of February 15 (fig. 7), March 11 (fig. 8) and May 20 (fig. 10), taken by ourselves after the operation, the outlines were plotted with discs of 0.5 cm. diameter, and we merely indicated by lines upon the charts that some vision to larger (2 cm.) discs was apparent in the previously blind temporal fields. As will appear from the observations of September 18, 1912 (fig. 11), and January 5, 1913 (fig. 12), we had by this time begun to record upon the same chart the outlines given by discs of graduated areas, from $\frac{1}{4}$ sq. cm. to 16 sq. cm.—an extension of the screen method of Bjerrum [2] [3] [4] and Rönne [17] [18] [19] used by them in cases of glaucoma and optic atrophy, adopted for our purposes to the perimeter.

Attention may be called to the fact that the earlier charts, not only our own but those of Dr. Weeks, failed to indicate a relative central scotoma, which in the light of subsequent experiences was in all probability present. Thus the field of the right eye, taken January 22 (fig. 6), should in all probability not have shown the macula clearly bisected, but should have indicated a relative central haziness, the existence of which, at the time, is reasonably assured by the lowered $\frac{20}{50}$ —vision.

It is occasionally indicated, even on these older and less carefully plotted charts (as shown in fig. 7), the patches of vision may be retained in the blind fields, or that vision in these fields may first return in patches—a matter which will be entered into more fully later on. Suffice it to say, we did not appreciate the significance of these islands until we came regularly to employ the graded discs.

TECHNIQUE OF PERIMETRIC EXAMINATIONS (C. B. Walker).

Though the methods of plotting fields which we have come to depend upon are applicable to all cases, the information to be gained therefrom is much greater in the group of anterior (chiasmal) lesions, to which these hypophysial cases belong, than in the cases of field defects due to central (cerebral) lesions. Thus if we make a primary

division of fields into (1) those taken in cases of anterior lesions and (2) those taken in cases of posterior lesions, it is notable that the line of cleavage between blind and seeing field is generally much sharper in posterior than in the anterior cases. For instance, it is the rule to find that a patient with homonymous hemianopsia of posterior origin fails to note the motion of objects, no matter how large, to the blind side of the fixation point until one edge projects into the seeing field, while a patient with an hemianopsia of anterior origin who shows a fairly sharp line of cleavage for small form and colour discs, may still be able to detect gross movements on the defective side of the field.

The representation on charts of the full functional capacity of the retina in these cases was not satisfactory with the ordinary equipment, on account of lack of uniformity. Accordingly a new series of discs was devised, which ranged in graduated sizes above and below the ordinary normal or 0.5 cm. disc. By the use of such a series we hoped to be able to trace fluctuations in the visual fields more accurately, and possibly get an index from the isopters of the different discs as to what the next stage would probably be.

In choosing a basis for our disc series it did not seem advisable to depart too radically from the system in general use, since most of the patients came from a distance with several previous fields indicating a progression of stages, and on their return home continued to have their fields plotted on the original basis. This serial method devised by one of us may be used both in the general manner with the perimeter and on the Bjerrum screen; but with the latter method the denomination of the visual angle fraction must be changed, since practically all the perimeters in this country are built on a radius of about 280 mm.

Our method, then, elaborated with especial reference to hypophysial cases and other progressive lesions, does not involve the use of a special perimeter, but the discs cover a considerably larger range, the largest being of such a diameter that further increase in size gives practically no added information in the defective areas. In order to have the test objects symmetrically disposed about a central point from which the measurements are taken and which lies as nearly as possible in the same focal plane as the fixation point, circular, flat discs are used, having only a knife edge, serving merely to protect the mat surface of the disc. The rimless feature of these discs is essential, since we have found, especially with small test objects with relatively large rims and handles, that motions of the carrier may be reported before the

test object itself is noted. With rimless discs and wire handles, even without repeated warnings to the patients, we are much more confident that reported motions are actually due to the test object.

Further, since the circle having the same diameter as the side of a given square has an area only three-quarters the area of the square, our discs are mentioned in terms of circular areas, in order to avoid confusion as to whether a square or circular test object has been used.

In regard to the size of the discs, it has been found that diameter ratios of 1 : 2, or what is the same thing, area ratios of 1 : 4, give readings most satisfactorily charted. The normal or 5 mm. disc being so commonly used, must be included in the series, and is therefore taken as a starting point. Above and below this size, the discs range in diameter ratio of 1 : 2. In all the charts herein presented, where four form peripheries are shown, the inside line always represents, unless otherwise stated, the normal disc, and the outer lines discs of increasing size in the given ratio.

On the back of each white disc is a green disc, and at the other end of the wire handles and at right angles to the white and green discs is another double disc of red and blue. This arrangement prevents the patient from seeing more than one disc colour at a time, and enables the observer to change the colours without the patient's being aware of his doing so.

It has not been found necessary to vary the testing apparatus from that usually employed, and mechanical perimeters have not been found to offer any advantage over the plain perimeter in taking fields as completely, accurately and rapidly as possible. It may be said that a special blinder is also used, fitted with two attachments by which a field may be taken on an eye having a central scotoma, if vision and fixation are good in the other eye.¹

There are certain theoretical considerations of interest in relation to the distribution of the fibres damaged by the pressure and of their terminals in the retina. Thus if it be assumed that when a visual nerve-fibre is subjected to pressure in any part of its path its function is first weakened before becoming entirely blocked, one may conceive, in the case of pressure against a bundle of fibres, of concentric zones of diminishing effect of the pressure. In the first zone would be found fibres entirely blocked or even destroyed; in the second zone some scattered normally functioning fibres might appear; in the third

¹ A more detailed description of these instruments may be found in an article recently published by one of us [20].

occasional entirely blocked or extremely depressed fibres might be found among those considerably depressed but still imperfectly functioning; outside of these zones a fourth zone of slightly depressed fibres would be located, and so on. If such zones were present in the nerve it would not be surprising if they disclosed themselves in the retina as zones of different stimulability, that is, if a defect in the form field were demonstrable with the normal sized disc, the defect recorded by a larger disc would be still smaller, and the distance between the two lines in the normal field would represent practically the difference in the disc radii, while in the defective region the lines would spread considerably apart, depending on the nature and degree of damage in the postulated zones.

A study of the fields before and after operation gives considerable evidence that atrophy of the visual fibres does not necessarily take place until they have been under pressure sufficient to block their function for six months or a year, or even longer. If a sharp atrophy or destruction of visual fibres has taken place no response to graduated discs in the defective area is expected, the larger discs being perceived only when their margins reach the line of cleavage between blind and seeing fields. In such visual defects there is obviously little hope of improvement. Altogether, then, field examinations in conditions and with changes of this sort would possibly not only add considerable information in regard to the functional capacity of the optic tract and retina, but would also, when a series of fields and time durations were available, give some evidence of the position, size and rate of growth of the lesion.

The method of Bjerrum involves the use of a black screen 2 metres square, at a distance of 2 metres from the patient. The test objects are spots 3 mm. and 6 mm. in diameter. At a distance of 2 metres the field for these test objects, although only 30° to 40°, may be considerably larger than the screen. Therefore, in order to confine the measurements to the area of the screen, the fixation point must be changed from point to point. To record the field reading on the chart the measurements of meridian and arc, ordinarily made direct from the perimeter, must now be actually measured on the screen for each reading with rule and protractor. The test object is recorded in terms of a factor which represents its visual angle, that is, $\frac{\text{diameter of disc}}{\text{distance from patient}}$, since this fraction multiplied by the factor $\frac{180}{\pi}$ gives the visual angle in degrees.

This method was adopted on account of the difficulty of making accurate discs below 1 mm. in diameter. If such discs could be made so as to represent visual angles of five minutes (about equal to $\frac{20}{20}$ vision) and less on the ordinary perimeter, several objections to the Bjerrum method would be obviated. These objections are, first, that the discs have a variable visual angle and focal plane as they are used at various points on the flat screen surface; second, that presbyopic patients cannot use their glasses to advantage for the middle distance of 2 metres, since they are made for 6 metres or for reading; third, the loss of illumination intensity due to the instance; and finally and most important, the readings are so laboriously made and recorded that as the patient grows fatigued results become unreliable.

We have been able to make discs of very small size, extending our series downward until the visual angle on the ordinary perimeter approaches one minute, very close to the limit of visibility. As was anticipated, the same results are obtained by this method as with the Bjerrum method, but with greater facility and rapidity. The area ratio is maintained at 1 : 4 throughout.

Thus we have devised similar methods of examining the areas both outside and inside the boundaries established by the normal disc. The larger discs are especially useful in giving added information concerning the residual functional capacity in a defect found by the normal disc. If this defect is of considerable extent the very small discs may not give much added information concerning the functional capacity of the remaining field, but it is when there is practically no defect to the usual discs that the very small discs may be found to give the most valuable, sometimes most unexpected information.

CASE REPORTS ILLUSTRATING STAGES OF BITEMPORAL HEMIANOPSIA.

The first draft of this paper was drawn up two years ago with the selection of twenty illustrative case reports from our Baltimore series. Significant of the improvement in our technical methods of perimetry is the fact that though several of these earlier cases are of unusual interest we, nevertheless, in this interval have come to supplant them, one by one, with more recent cases as inaccuracies in our former methods became apparent. Possibly, should we delay for another two years we might have the same feeling in regard to our present charts. However, the following thirteen records which we have finally chosen may

serve as fairly satisfactory examples of the conditions to which we wish to call attention.¹

The cases will be divided into two groups: (1) those in which the hemianopsia was produced by a lesion, usually a glandular struma so-called, originating within the sella—a condition favourable for a transphenoidal operation; and (2) those in which it was produced by a suprasellar tumour—which does not necessarily deform the sella turcica, whatever it may do to the chiasmal cross-roads themselves.

(a) *The intrasellar tumours causing bitemporal hemianopsia.*—It will be observed in the following nine case reports (Case 2 to Case 10) that an attempt is made to present the cases serially so that one or the other eye at the time of the earliest observation is at a stage slightly in advance of that in the preceding case. In the following example (Case 2) when the patient was first seen the fields were regarded as normal, and consequently the case is one of the several that are not included in the given statistics, which, as has been told, were based on the conditions found at the patient's first admission. It is an illustration of the earliest field deformation which we have come to recognize as typical.²

Case 2 (P.B.B.H., Surg. No. 1484).—Acromegaly with early unilateral field defect in Stage I. Operation. Improvement.

November 15, 1913.—Admission of Miss E. A. C., a school teacher, aged 35, referred to by Dr. H. B. Hawley, of Syracuse, N.Y. Typical early acromegaly, with enlarged sella, headaches, amenorrhœa, asthenia and ocular fatigue.

Examination of eyes.—Fundi, fields, acuity, &c., show no abnormality.

July 10, 1914.—*Readmission*, owing to advance in symptoms. *Fields* (fig. 13): Left eye shows Stage I, with relative paracentral scotoma and lowering of acuity to $\frac{2}{30}$; right normal.

July 16.—*Transphenoidal operation.* Partial removal of tense chromophile struma. Immediate subjective improvement; discharged in ten days with V.O.S. $\frac{2}{30}$, but no change in field peripheries when they were taken on July 22.

August 26.—*Returns for examination.* Great improvement in all respects, with rapid diminution of the pituitary myxœdema. The left field shows widening of all peripheries, though there is still a slight slant of the upper temporal area. There is no trace of the scotoma even to minute discs. V.O.S. $\frac{2}{30}$, V.O.D. $\frac{1}{18}$.

¹ In the case records used in this report, those from the Baltimore series are given their J.H.H. surgical number, and we wish to express our obligation to the Johns Hopkins Hospital for the privilege of including them here.

² It may be said that in the succeeding charts the colour peripheries are (unless otherwise mentioned) always plotted to the normal test object; and that a single outline for the form field is also taken with the same sized disc. When the graded discs are used the peripheries from within outward represent, serially, registrations from $\frac{1}{2}$, 1, 2, and 4 cm. discs.

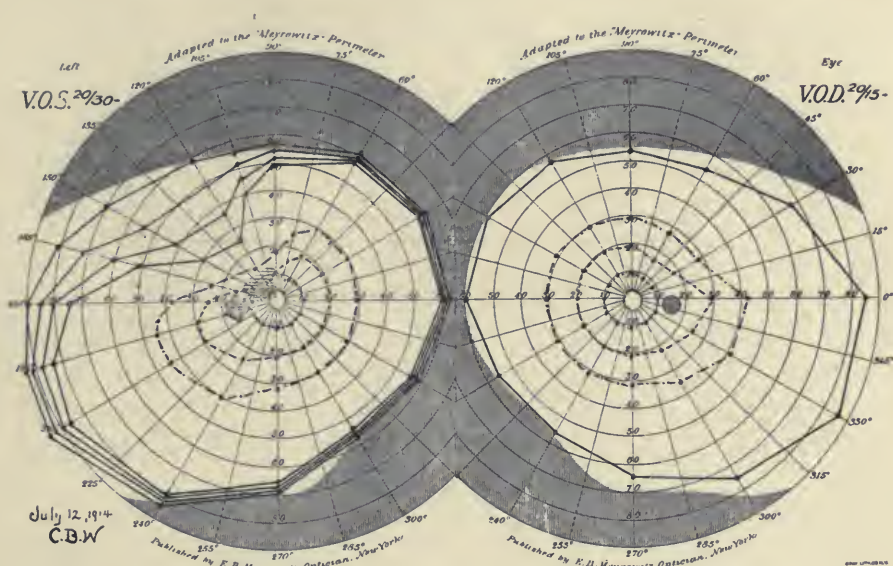


FIG. 13.—Case 2. Fields of July 12, 1914, showing on the left the typical outlines of the form field of Stage I, as plotted by the four graduated discs $\frac{1}{4}$ sq. cm. to 16 sq. cm.

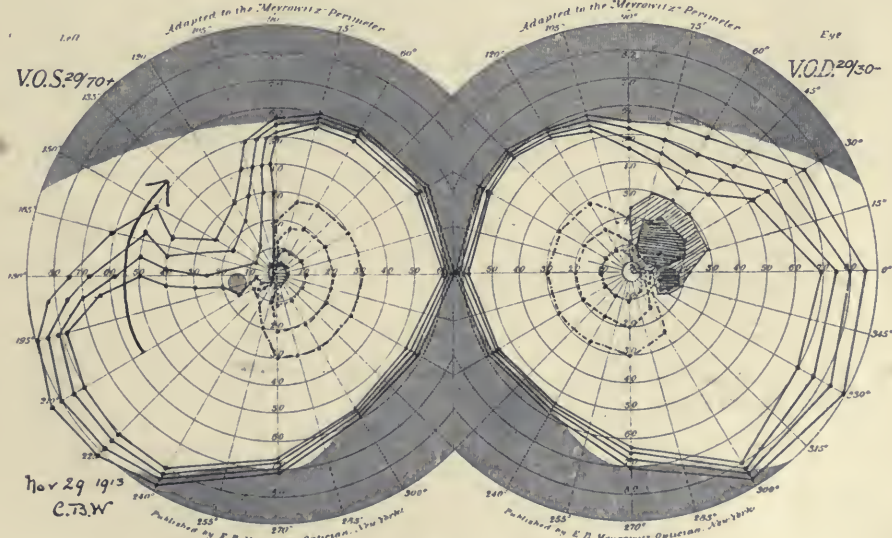


FIG. 14.—Case 3. Fields of November 29, 1913, three days before operation. Advanced Stage II on left, and advanced Stage I on right. In left field arrow shows direction of post-operative recession with envelopment of what will be the subsequent scotoma (cf. fig. 15).

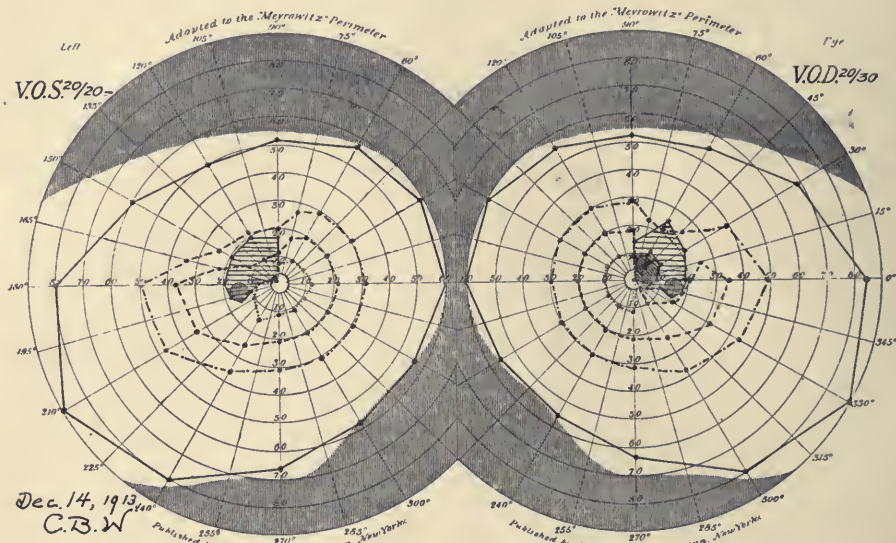


FIG. 15.—Case 3. Fields of December 14, 1913, twelve days after operation, showing recession to early Stage I, with persistent relative scotomata.

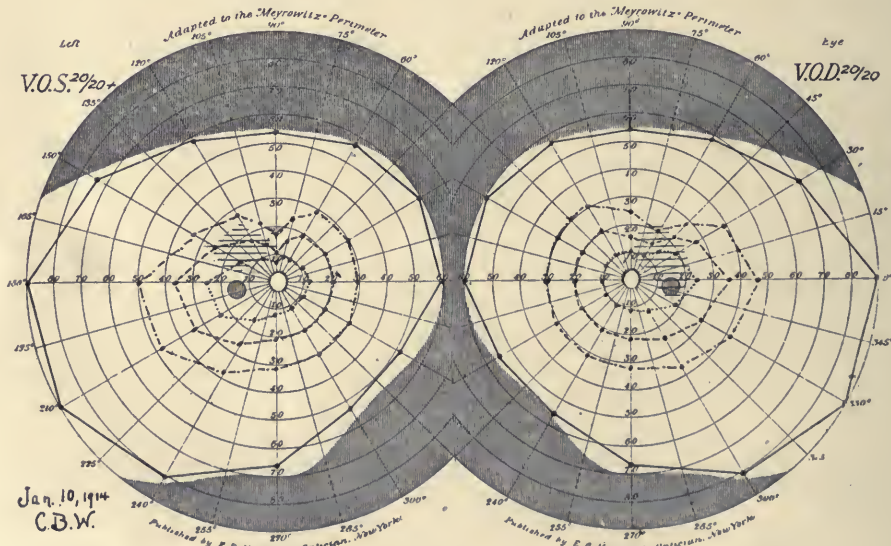


FIG. 16.—Case 3. Fields of January 10, 1914, six weeks after operation. Practical return to normal.

Comment.—In view of the normal right eye, one cannot be certain of course, in such a case that the condition might not have eventually proved to be an homonymous one. There have been two or three very similar cases in the series.

The following example shows an advance to Stage II at the time of admission.

Case 3 (P.B.B.H., Surg. No. 1135).—Acromegaly with field defects approaching Stage II. Operation with recession to normal.

November 26, 1913.—Admission of H. A. E., aged 23, a signal-tower operator, referred by Dr. W. O. Paul, of Dorchester, Mass. Typical early acromegaly with faulty vision for five or six months, headaches, enlarged sella, &c.

Examination of eyes.—Pupils show practically normal reactions. No nystagmus, exophthalmos, von Graefe, or limitation in movements. *Fundus*: O.U. Optic disc pale but with a slight blush of injection present. Nasal side of disc is paler than normal but still has more colour than temporal side. Margins slightly blurred by a low grade of œdema and some injection. Very slight venous congestion. Fundus otherwise clear. *Fields* (fig. 14) show an advanced Stage II on the left, and on the right an advanced Stage I with practical hemiachromatopsia, an upper temporal slant of the form fields and a paracentral scotoma in the quadrant. V.O.S. $\frac{2}{3}$, V.O.D. $\frac{3}{8}$ —.

December 2.—*Operation.* Usual transphenoidal procedure with partial removal of large chromophobe struma. Uneventful recovery with prompt subjective improvement in vision.

December 14.—Fundus has lost its injection. *Fields* (fig. 15) show restoration, both right and left, to early Stage I. V.O.S. $\frac{2}{3}$ —, V.O.D. $\frac{3}{8}$ —. *Discharged.*

January 10, 1914.—Reports for examination. *Fields* (fig. 16) practically normal though a slight trace of the scotomata is still demonstrable. V.O.S. $\frac{3}{8}$ +, V.O.D. $\frac{3}{8}$.

January 20.—Has returned to his post as a signalman, on night duty, having successfully passed the imposed rigorous tests for vision.

Comment.—The charts of this and of some of the immediately following cases indicate how it is that a greatly enlarged blind spot or a central scotoma persists after the closing in of the form fields, which spread upward in the direction of the arrow (fig. 14) and fuse around the paracentral area where the fibres seem to suffer most.

The following case is an example of post-operative recession in a patient admitted in Stage III.

Case 4 (P.B.B.H., Surg. No. 972).—Hypopituitarism with optic atrophy and field defects in an advanced Stage III. Operation with recession to Stage I.

February 28, 1914.—Admission of Carl S., aged 49, a watchmaker, referred

by Dr. A. Ziegler, of Plainfield, N. J. A typical example of pituitary insufficiency, with large eroded sella, adiposity, headaches and subjective failure of vision for eight months, beginning in the left eye and two months later in the right. Progressive failure.

Examination of eyes.—Slight exophthalmos. Pupils show normal reactions. *Fundus*: Temporal portion of discs paler than normal, but might not be noted on casual examination. *Fields* (fig. 17) show typical and fairly symmetrical advanced Stage III, which particularly on the left and to the smallest disc approaches Stage IV. V.O.S. $\frac{20}{100}$ —, V.O.D. $\frac{20}{50}$ +.

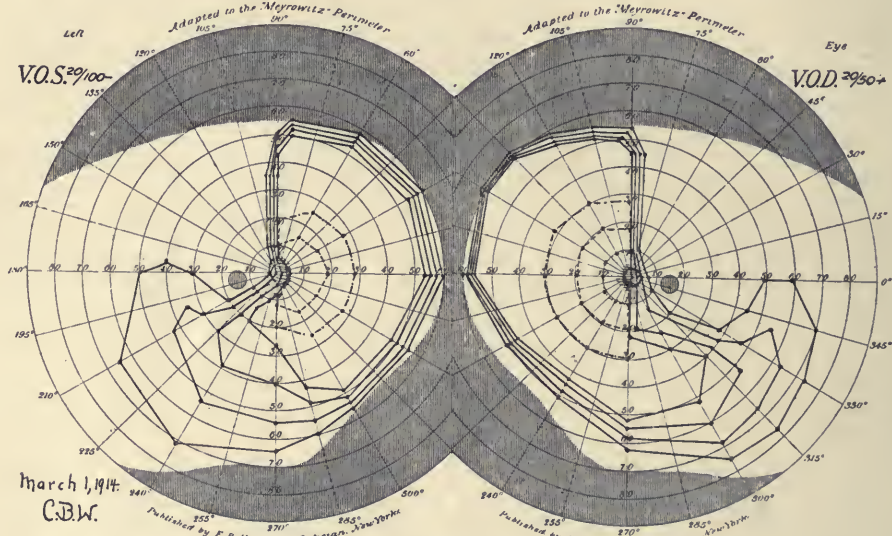


FIG. 17.—Case 4. Fields of March 1, 1914, four days before operation. To the smaller discs the condition is seen to be almost in Stage IV with vertical meridian.

March 5.—Operation. Usual transphenoidal approach with extensive extirpation of soft chromophobe struma. Uneventful recovery with prompt subjective improvement in vision.

March 10.—Fields (fig. 18) are widening to Stage III on the left and Stage II on the right. V.O.S. $\frac{20}{70}$ +, V.O.D. $\frac{30}{50}$.

March 16.—Fields show further improvement (fig. 19) with fusion of circumferential peripheries to 1 sq. cm. discs. V.O.S. $\frac{30}{50}$ —; V.O.D. $\frac{20}{50}$ —. Discharged.

Comment.—Of this typical retrogression in cases no further advanced than Stage III there have been several examples in the series. Though at the time of the patient's discharge eleven days after the operation, the temporal peripheries (fig. 19) had not fused to the $\frac{1}{4}$ sq. cm. (that

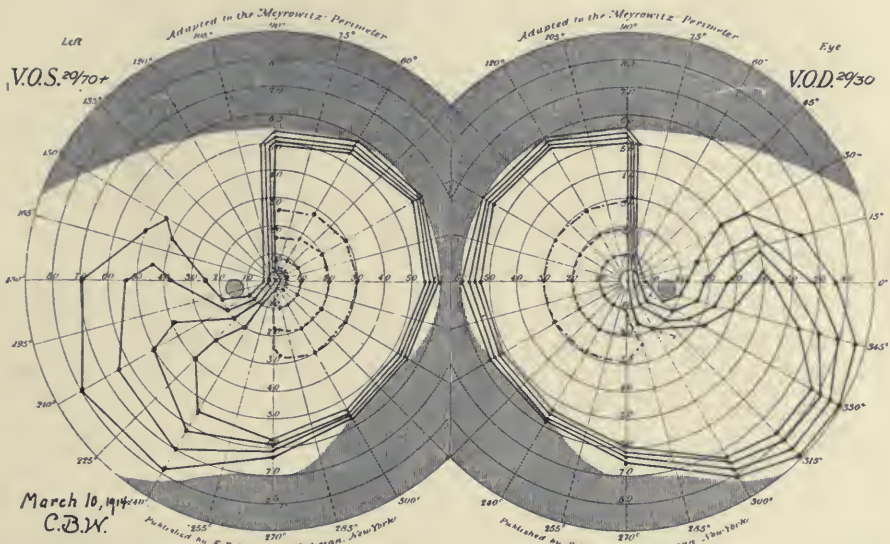


FIG. 18.—Case 4. Fields of March 10, 1914, five days after operation, showing recession to Stage III on the left, and toward Stage II on the right.

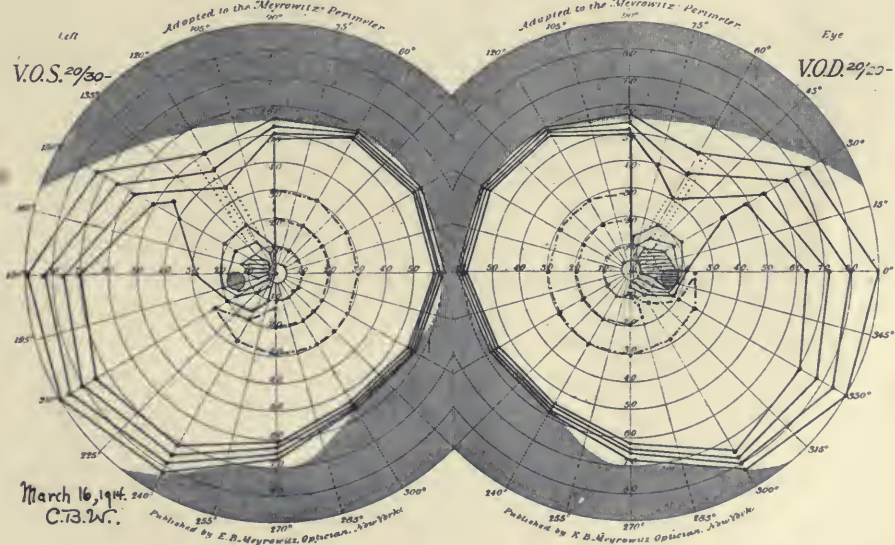


FIG. 19.—Case 4. Fields of March 16, 1914, eleven days after operation, showing fusion of form peripheries to discs of 1 sq. cm. and over, a relative paracentral scotoma for each of them remaining. Dotted lines connect the separate scotomata with the periphery for corresponding disc.

is to the normal) test object, they had fused to the larger discs in the series. In a patient at this stage, therefore, casually examined by the usual 1 cm. disc so often employed in perimetry, the outlines might easily have been regarded as normal, and as likely as not the relative paracentral scotomata shown to be present for the serial discs would have been overlooked. It is clear, of course, that the larger the disc the smaller will be the recorded size of the scotoma. Unfortunately no opportunity for subsequent observations in this case was afforded, and it is quite possible that completely normal outlines were attained.

Cases admitted in Stage IV.—We now come to Stage IV, representing the text-book stage of hemianopsia. Here apparently in many cases the condition lingers, and to this may possibly be attributed the fact that it has so long been regarded as the typical stage of the process. At this stage, moreover, one begins to have some misgivings in regard to restoration, a matter which doubtless depends on the duration of the pressure. In one patient who was seen by one of us five years ago in an advanced Stage III and who declined operation [6], the condition has only just advanced beyond Stage IV, but with so great a lowering of acuity that he eagerly sought the operation which had formerly been advised. This has recently been performed, but despite the thorough evacuation from the lower sella of its soft struma, there has been no immediate improvement in vision such as would have been expected after a similar operation performed earlier in the disease.

Provided, therefore, that the pressure has not been of too long standing, patients in this stage of hemianopsia may slowly improve, as exemplified by Case 1 recorded above, and occasionally the improvement may be very rapid; in some exceptional cases, indeed, normal outlines may be plotted a few days after an operation. This has happened twice in the series, both cases being those in which a cyst was encountered and drained and in which the hemianopsia had been of brief duration—a matter of months rather than of years.

The following case, though belonging in the amaurotic group owing to the left blindness, is one in which the seeing eye, were reliance placed solely on the usual normal disc, would be regarded as showing a typical hemianopsia (barring the mid-temporal field patch, to which further reference will be made). The serial discs, however, not only show that the condition is short of Stage IV, but also how it is that with returning vision the isolated island becomes incorporated in the widening field plotted with the normal ($\frac{1}{4}$ sq. cm. or 0.5 cm.) disc which had revealed the island.

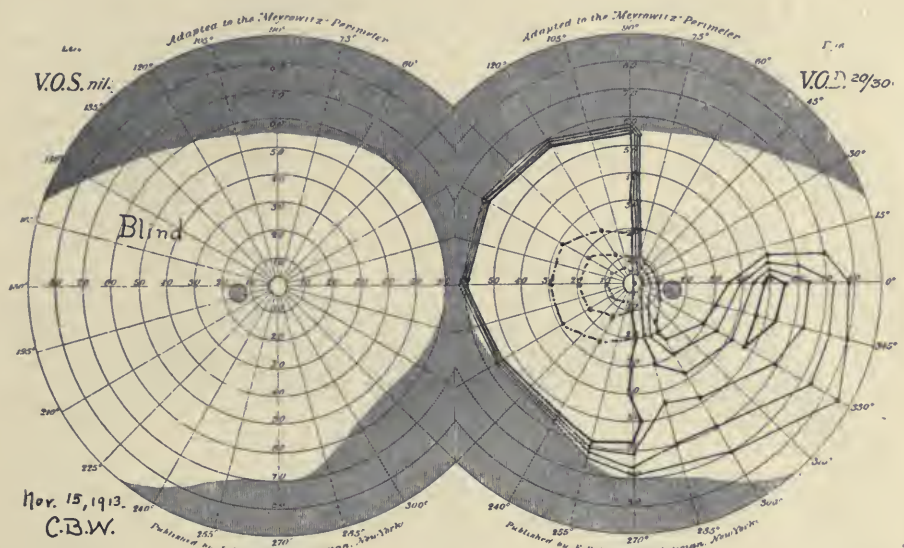


FIG. 20.—Case 5. Fields of November 15, 1913, five days before operation. O.S., Stage VIII; O.D., just short of Stage IV. Note island of retained vision to normal $\frac{1}{4}$ sq. cm. disc.

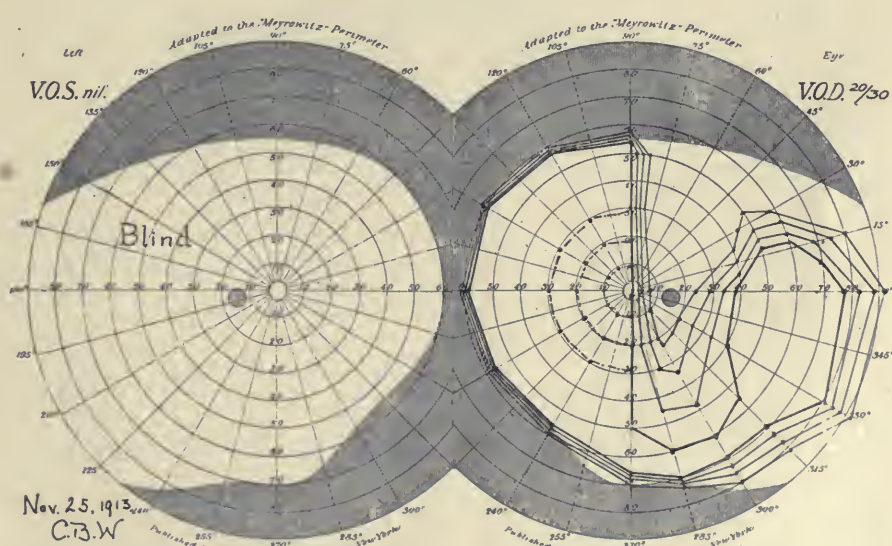


FIG. 21.—Case 5. Fields of November 25, 1913, five days after operation, showing incorporation of former island in lower nasal outshoot from field to $\frac{1}{4}$ sq. cm. disc.

Case 5 (P.B.B.H., Surg. No. 578).—*Hypopituitarism with primary optic atrophy. Left blindness; right eye short of Stage IV. Operation with improvement.*

November 13, 1913.—Admission of William S. M., aged 36, a mechanical draughtsman, referred by Dr. S. J. Wood, of Cape Town, South Africa, through Drs. James T. Taylor and J. Herbert Fisher,¹ of London. A typical example of adult adiposo-genital dystrophy with headaches, sellar distension, polyuria, asthenia, hypotrichosis, &c.

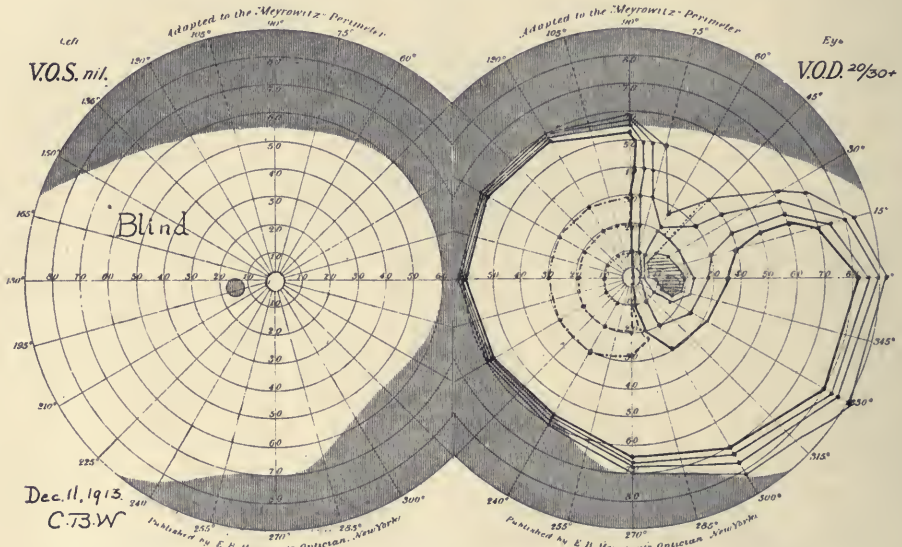


FIG. 22.—Case 5. Fields of December 11, 1913, three weeks after operation, to show recession to an advanced Stage II. Scotomata to the 2 and 4 sq. cm. discs.

Vision began to fail in the left eye about February, 1911, advancing through a temporal hemianopsia to blindness in one year. The right eye was first subjectively affected in June, 1912, seventeen months ago, and has progressed to its present condition.

Examination of eyes.—Pupils wide. *Fundus*: Discs pale, atrophic, moderately pigmented, 7 to 8 D. myopia. *Fields* (fig. 20): No vision on the left; right shows, to the normal $\frac{1}{4}$ sq. cm. disc, a complete hemianopsia with vertical meridian and a retained temporal patch in addition. This patch is concentrically enveloped in the three successive outlines plotted with larger discs. No relative central scotoma. V.O.S. nil, V.O.D. (corrected) $\frac{20}{30}$.

November 20, 1913.—*Operation.* Usual transphenoidal procedure with evacuation of large amount of soft chromophobe struma. No complications.

¹ Mr. Fisher [14] has already recorded the earlier progress of this case when there was still nasal vision in the left eye and the right had normal fields.

November 25.—*Fields* (fig. 21): There is widening of the lower temporal areas and the island has become incorporated in the offshoot from the lower nasal field.

December 2.—Further widening of fields demonstrated.

December 11.—*Fields* (fig. 22) on this date in fairly typical Stage III. V.O.D. (corrected) $\frac{3}{8}$ +. Patient discharged. No subsequent fields possible. Writes of further improvement.

The following case, though it also belongs in the amaurotic group owing to the Stage VIII condition of the left eye, will serve as another illustration of a condition similar to the above though slightly more advanced, for the island here is completely isolated even for large discs.

Case 6 (P.B.B.H., Surg. No. 24).—*Hypopituitarism* (Fröhlich type) with optic atrophy. Left blindness: right eye in Stage IV. Operation. Restoration to Stage VII left, and normal right.

February 25, 1913.—Admission on the recommendation of Dr. F. O. Nagle, of Philadelphia, of R. E. S., aged 23, a recent graduate in medicine. A typical example of adiposo-genital dystrophy (typus femininus). Three years before, during his medical course, his vision began to fail. He brings a series of perimetric charts taken at intervals since that time. Though too roughly plotted to be of value for our purposes they nevertheless show sufficiently clearly a bilateral advance from upper temporal defects to a temporal hemianopsia on the right and to complete blindness on the left, where vision was completely lost by February of 1912. Specific treatment, neosalvarsan, &c., without avail.

Examination of eyes.—No exophthalmos, diplopia, nystagmus, or extrinsic muscular disturbance. Pupils slightly dilated; left larger than right. Direct pupillary reaction present on the right, absent on left; indirect reaction present on left, absent on right; hemiopic reaction (rotary shutter) present on right. Refixation (Wilbrand test by use of special electric lights) retarded. Pseudo-refixation present. *Fundus*: O.U., optic disc wide, pale, and sharply outlined. Optic cup wide and shallow. Lamina cribrosa easily made out, but not as sharp as in a toxic primary atrophy. Faint layer of new tissue on disc but no perivascular streaking. Fundus otherwise in good condition. *Fields* (fig. 23): No vision on the left. On the right a hemianopsia with central scotoma, typical in all respects of Stage IV except for the small patch of vision on the horizontal meridian in the midtemporal field. V.O.D. $\frac{2}{8}$.

March 3.—*Operation.* Typical transphenoidal procedure with extensive removal of soft chromophobe struma. Uneventful recovery, with immediate (on recovery from anæsthetic) subjective improvement in vision.

March 6 (third day).—*Field* (fig. 24) on the right has greatly widened. A tongue for the normal $\frac{1}{4}$ sq. cm. disc has shot out from the lower side and

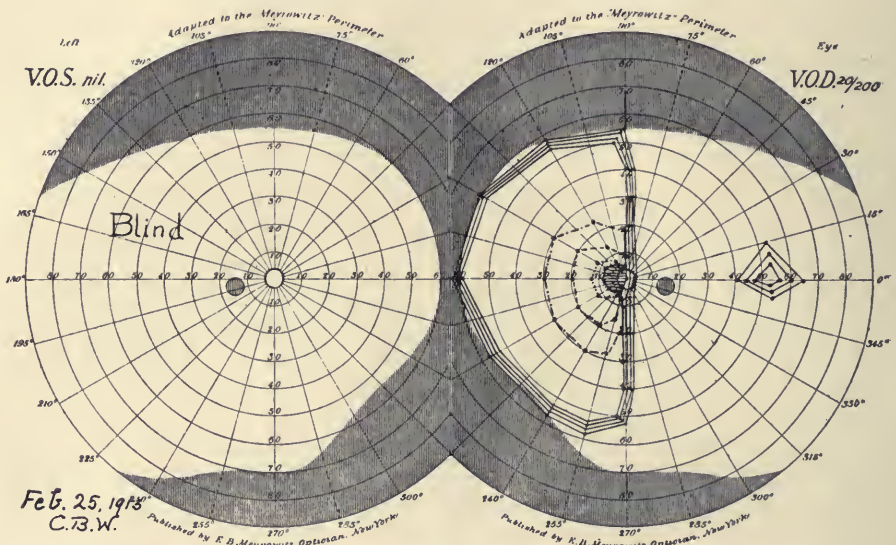


FIG. 23.—Case 6. Fields of February 25, 1913, showing condition before operation. O.S., Stage VIII; O.D., Stage IV. Note retained island in right temporal field.

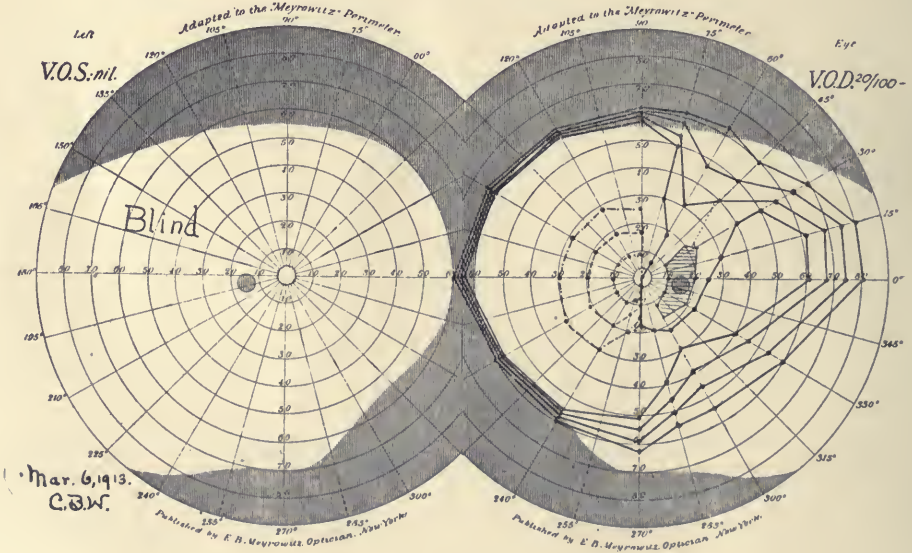


FIG. 24.—Case 6. Fields of March 6, 1913. Three days after operation, showing early great improvement. Note development by widening fields of isolated patch shown in fig. 23.

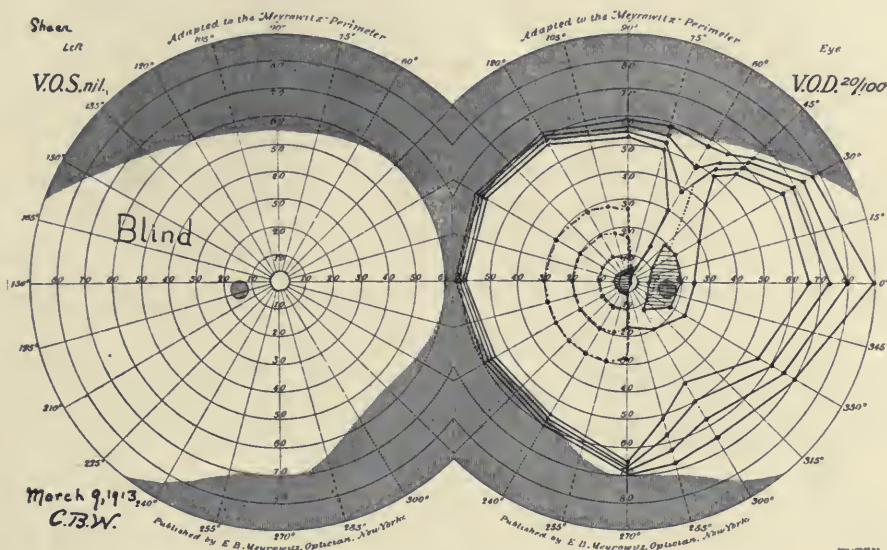


FIG. 25.—Case 6. Fields of March 9, 1913, six days after operation. Paracentral scotoma to 1 sq. cm. disc persists. Note approaching fusion of peripheries to $\frac{1}{4}$ sq. cm. disc.

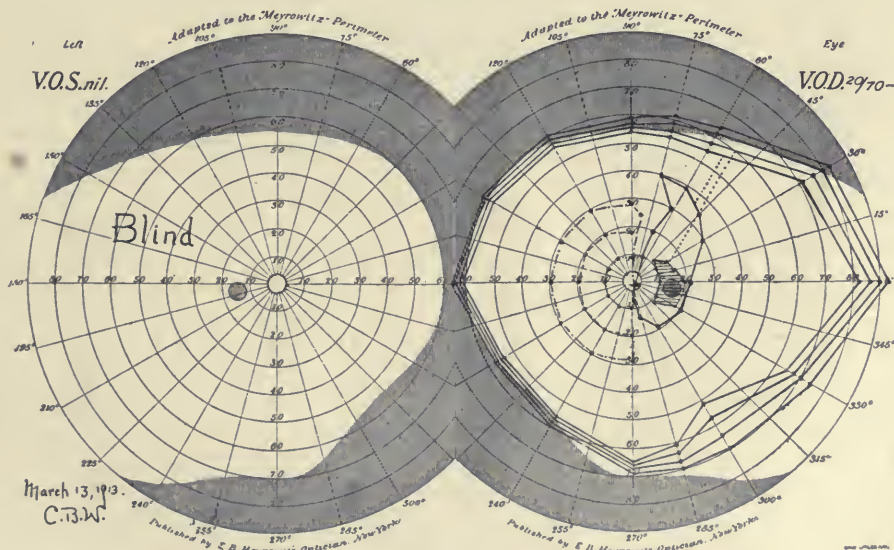


FIG. 26.—Case 6. Fields of March 13, 1913, ten days after operation, showing peripheral fusion of the field to the normal $\frac{1}{4}$ sq. cm. disc, leaving a relative paracentral scotoma for this as well as for the 1 sq. cm. disc.

enveloped the patch of preserved vision mentioned above. To larger discs (1 sq. cm. and over) the peripheral field, advancing from the sides, has fused around the upper temporal quadrant enclosing a scotoma for the 1 sq. cm. disc. V.O.D. $\frac{20}{100}$.

March 9 (sixth day).—*Fields* (fig. 25): A still further improvement shown, though fusion not quite complete as yet to the normal $\frac{1}{4}$ sq. cm. disc. V.O.D. remains at $\frac{20}{100}$, owing to the central scotoma.

March 13.—The peripheral field (fig. 26) has fused even to the smallest disc, leaving relative paracentral scotomata to the two smaller ($\frac{1}{4}$ and 1 sq. cm.) discs. V.O.D. $\frac{20}{70}$ — *Discharged*.

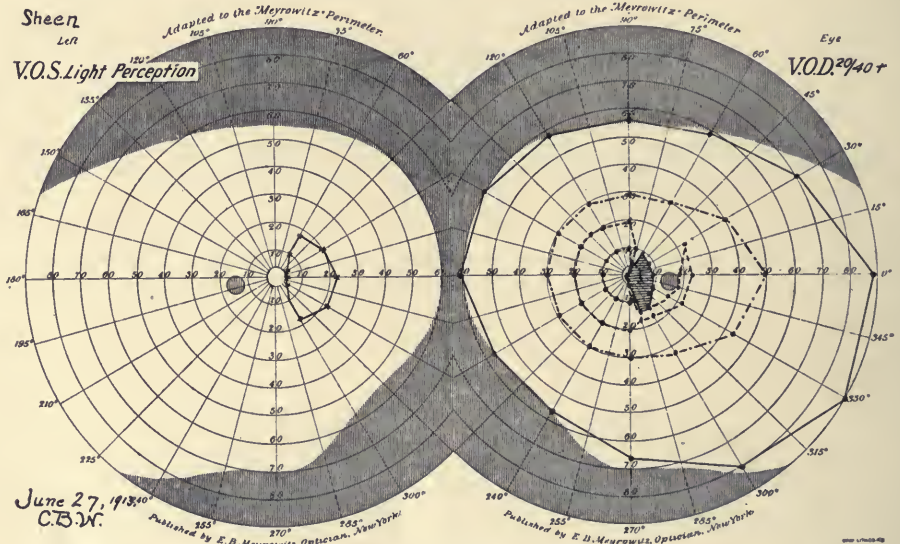


FIG. 27. Case 6. Fields of June 27, 1913, eight weeks after operation, showing normal conditions (apart from the scotoma and the red and green peripheries) largely regained on the right, and return of vision (Stage VII) on the left.

April 26, 1913.—*Reports for examination.* *Fields* show further improvement with an unexpected return of the pupillary reaction and of a nasal patch of vision on the left, where blindness had been complete since November of 1912. On the right the peripheries are fairly normal, with a persisting enfeeblement of central vision and a relative paracentral scotoma to both $\frac{1}{4}$ and 1 sq. cm. discs. V.O.D. $\frac{20}{40}$ —.

June 27, 1913.—*Reports for examination.* *Fields* (fig. 27) improved over last note. The patch of vision on the left persists unchanged. On the right the form periphery is normal and also the blue periphery to $\frac{1}{4}$ sq. cm. discs. The red field projects on to the lower temporal field and there is only half vision for green. There is also a small relative scotoma for the $\frac{1}{4}$ sq. cm. disc. V.O.S., light perception, V.O.D. $\frac{20}{40}$ +.

Subsequently, though there was some further progress it was very slow, with but little variation in the later fields. However, by October the acuity had risen to $\frac{20}{40}$.

The fields of October 16, 1913, show a persistence of the scotoma, accounting for the slightly lowered vision in what would otherwise be a normal field and eye. This observation represented the high tide of improvement, and the condition held there for the following nine months. At the last examination, August 4, 1914, a slight lowering of the acuity was noted, with a measurable increase in size of the scotoma, but otherwise the fields had remained as in June of 1913.

Comment.—As in the preceding case, here again an interesting feature of the blind temporal field is the patch of retained vision on the horizontal meridian seen on the pre-operative charts; and the manner in which this small area is engulfed by the upward swing of the tongue of vision in the process of recession to Stage III is very clear in the post-operative series. Doubtless had an observation been made on the first or second day after the operation, the transition would have been still more apparent.

In the following case the manner in which such a patch becomes incorporated in the widening field is particularly clear. It shows, moreover, not only that these patches may be bilaterally represented, but also that in the process of restoration such an isolated patch may chance to be recorded if the examination happens to coincide with its appearance. Unfortunately we were only able to observe this patient for less than three weeks, and we are unaware of the later changes.

Case 7 (Corey Hill Hospital).—Hypophysial struma with optic atrophy. Fairly symmetrical bitemporal defect short of Stage IV. Operation. Improvement.

December 17, 1912.—Admission of G. E. H., aged 32, a business man, referred by Dr. C. L. Chambers, of Detroit. There were very few glandular manifestations in the case, the greatly distended sella and the bitemporal hemianopsia being the chief distinguishing features.

He had had "trouble with his eyes" for six or seven years, and had consulted numerous specialists, who had changed his glasses. There had been occasional periods of diplopia.

Examination of eyes.—Pupils equal and reactions normal. *Fundus* shows considerable pallor of nerves. *Fields* (fig. 28) show a fairly symmetrical bitemporal defect approaching Stage IV, with an island of vision for the largest disc alone on the right temporal field, and also a central scotoma. V.O.S. $\frac{20}{40}$, V.O.D. $\frac{20}{40}$.

January 18, 1913.—*Operation.* Sellar decompression without removal of struma. Uneventful recovery.

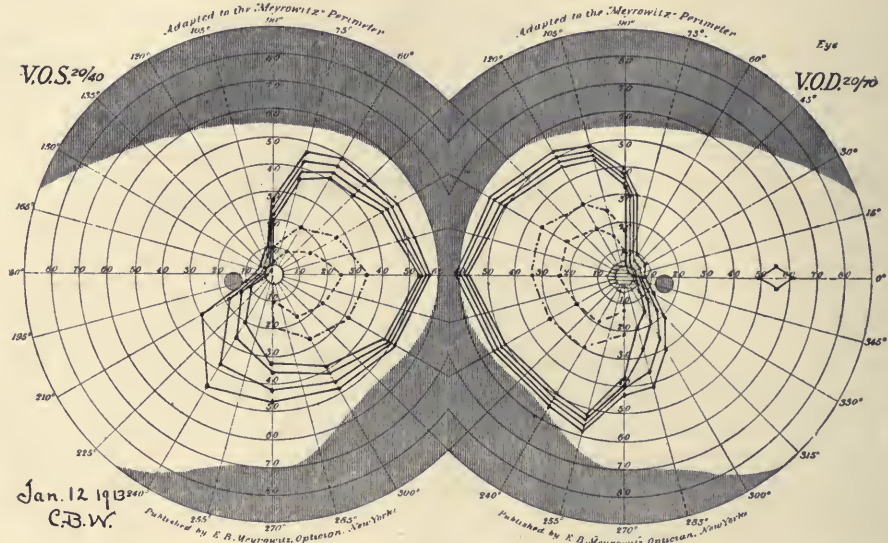


FIG. 28.—Case 7. Fields of January 12, 1913, before operation. Both eyes just short of Stage IV. Note island of vision in right temporal field.

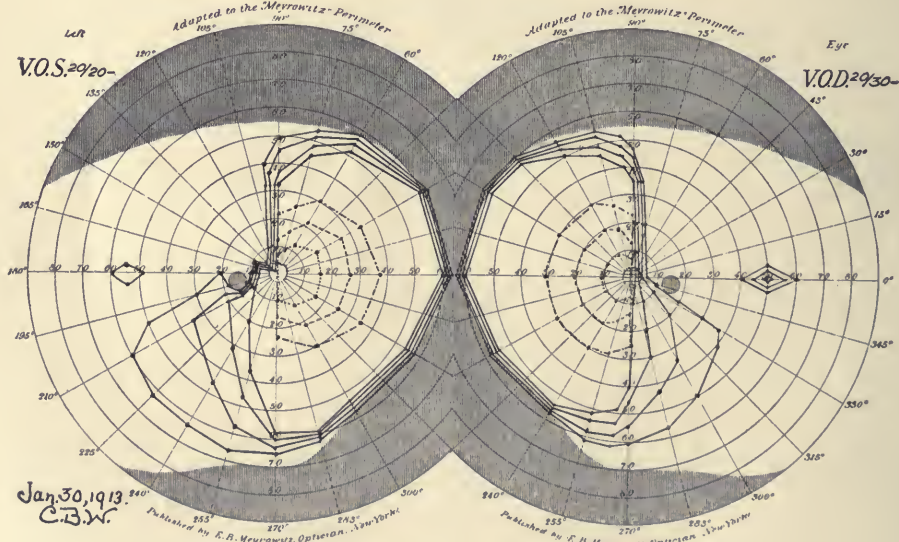


FIG. 29.—Case 7. Fields of January 30, 1913, twelve days after operation, showing widening of the lower temporal peripheries and the appearance of a symmetrical island on the left.

January 26.—Fields show some widening of the peripheries, and the acuity has considerably improved. V.O.S. $\frac{20}{20}$, V.O.D. $\frac{20}{20}$.

January 30.—Fields (fig. 29) show further widening and the appearance of an island for the largest disc alone in the left temporal field, while the island on the right has regained vision for smaller discs. Acuity unchanged. Patient discharged.

February 5.—Reports for examination. Fields (fig. 30) show further change with approach to Stage III and incorporation of the island on the right in the widening field for the largest disc. V.O.S. $\frac{20}{15}$, V.O.D. $\frac{20}{20} +$.

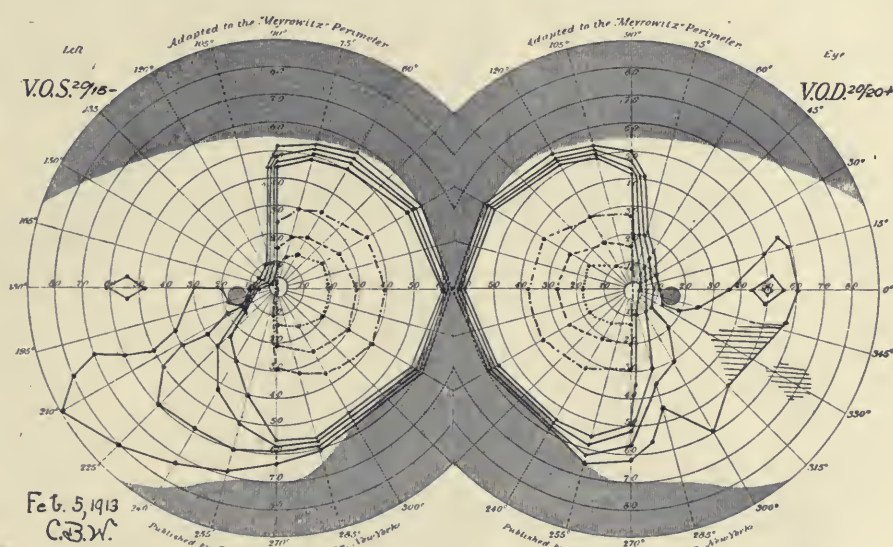


FIG. 30.—Case 7. Fields of February 5, 1913, eighteen days after operation, showing further recession toward Stage III, with engulfing of island on the right by the 16 sq. cm. disc.

Comment.—That these patients do not all do as well after operation as the foregoing seven cases might seem to indicate is shown by the following example in which the condition advanced despite the two operations which were undertaken. The case has been chosen to illustrate Stages V and VI of the process, and though it has been taken from the amaurotic group, the history shows that a bitemporal defect has once been observed. Explanations for the failure of improvement probably lie in the long duration of the process and in the presumable suprasellar extension of the struma.

Case 8 (P.B.B.H., Surg. No. 37).—*Hypopituitarism. Chromophobe struma with probable suprasellar extension. Optic atrophy. Stage V advancing to Stage II despite operation.*

October 16, 1912.—Admission of J. D. A., aged 52, a salesman, recommended by Dr. C. M. Carlow, of Minneapolis.

An example of advanced adult adiposo-genital dystrophy with hypotrichosis, obesity, impotence, somnolence, psychoses, complete loss of sellar outlines, &c.

Subjective loss of vision was first observed in the fall of 1910, a perimetric examination at the time showing left hemianopsia; right eye normal. By December of 1911 vision began to fail on the right, and in June of 1912 a bitemporal hemianopsia was present (Dr. Casey A. Wood). The condition progressed, and three weeks before admission vision had completely faded on the right, so that though the process began on the left, the right eye finally outstripped the left.

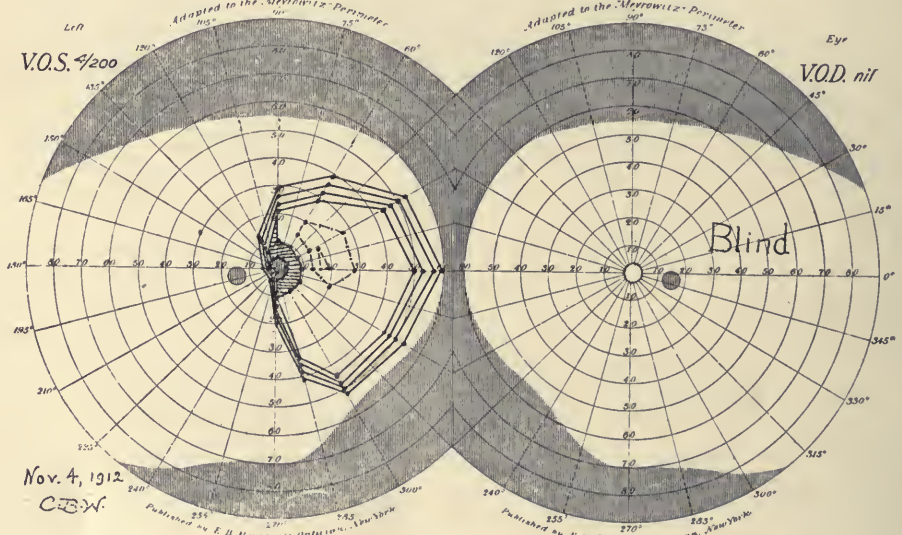


FIG. 31.—Case 8. Fields of November 4, 1912, showing the Stage V condition at the first admission unaltered by operation.

Examination of eyes.—No exophthalmos; movements free and complete; no nystagmus. O.D. turns in slightly. Right pupil dilated and inactive to direct light, but active consensually with O.S. Pupil O.S. smaller, and gives good direct, but no consensual reaction. *Fundus.* Extreme pallor. Lamina cribrosa hazily seen. Typical "primary optic atrophy." *Fields* (fig. 31) show an advanced Stage V on the left; colours in a small area apparent only to large discs. V.O.S. $\frac{4}{200}$, V.O.D. nil.

October 21, 1912.—*Operation.* Usual transphenoidal procedure with extirpation of large amount of soft chromophobe struma. Uncomplicated recovery. On the morning after operation some light perception in the blind eye, but

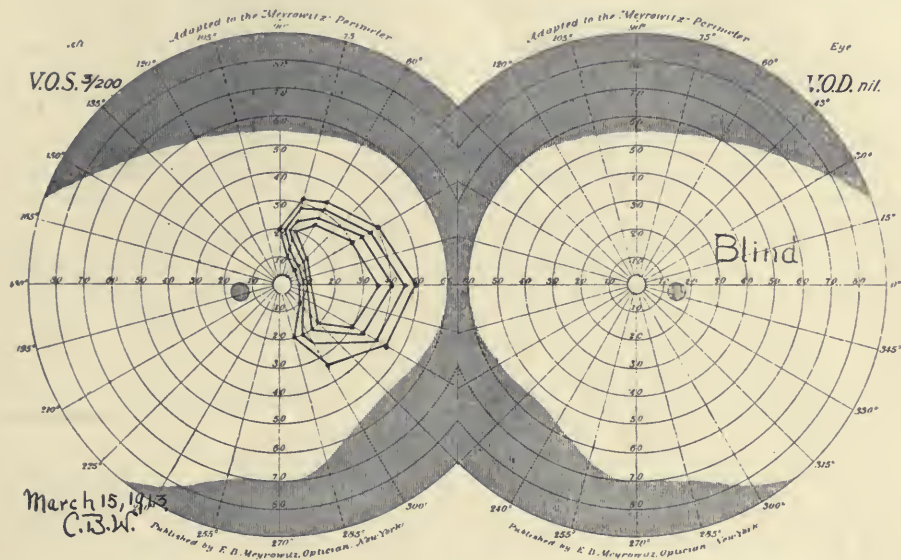


FIG. 32.—Case 8. Fields on second admission, March 15, 1913, showing advance to Stage VI.

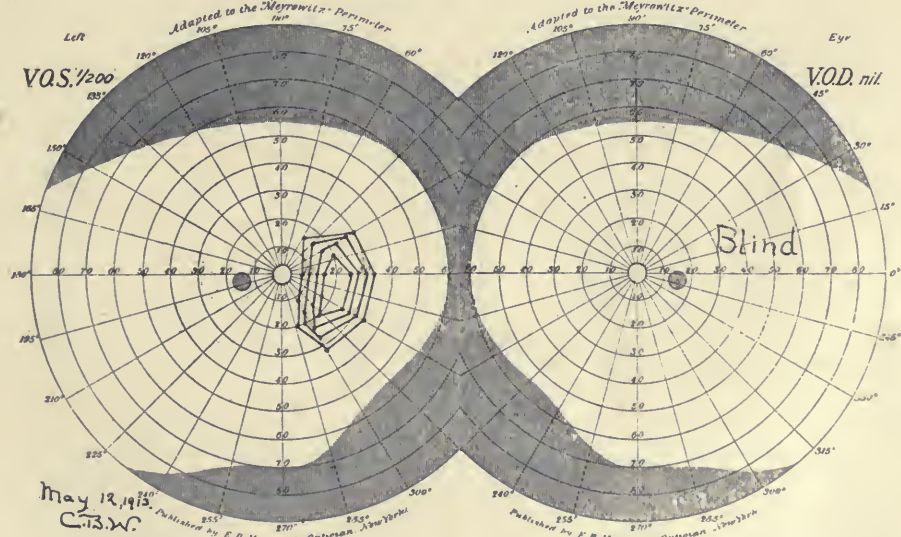


FIG. 33.—Case 8. Fields of May 12, 1913, after second operation, showing advance to Stage VII.

this was soon lost. Fields of *October 26* and *November 4* show a slight widening of the peripheries, but no significant change. Discharged.

March 15, 1913.—Readmitted. His general condition, despite pituitary feeding, has progressed unfavourably. The vision has remained almost stationary until the past few weeks, since when it has failed rapidly. The *field* has considerably shrunk, approaching Stage VI (fig. 32). V.O.S. $\frac{2}{200}$.

April 14, 1913.—Second operation. Transphenoidal route re-entered, with further extensive removal of intrasellar struma. Uneventful recovery, but progressive constriction of fields (fig. 33) and a further lowering of vision to V.O.S. $\frac{1}{200}$ at the time of discharge, *May 12, 1913*.

September 2, 1913.—By letter. Mere light perception. Symptomatic evidences of intracranial involvement.

Comment.—The above case is given largely to emphasize the need of early operation in the presence of a greatly enlarged sella, for this condition represents a comparatively simple surgical problem. With delay an intracranial invasion by the oedematous struma is likely to occur, and there is then little hope for preservation of vision, or, indeed, for a long preservation of life. However, under favourable circumstances, even an advance to Stage VII may not be incompatible with improvement, as the succeeding history will show. It illustrates a rapid recession after operation from Stage VII to Stage III—an unusual degree of improvement in our experience after such an extensive involvement of the nerves has become apparent.

Case 9 (P.B.B.H., Surg. No. 1A).—Hypopituitarism with chromophobe struma, optic atrophy, adiposity, &c. Operation. Recession from Stage VII to Stage III.

January 1, 1913.—Admission of A. S., aged 61, proprietor of a restaurant, recommended by Dr. F. W. Marlow, of Syracuse.

A typical example of hypophysial adiposity with advancing blindness and a widely distended, largely absorbed sella. Failing lateral and central vision had been observed for one year. A month before admission the fields (Dr. Marlow) showed a fairly symmetrical bitemporal defect in Stage IV.

Examination of eyes.—No exophthalmos, von Græfe or strabismus. Slight nystagmus. Pupils react to light, directly and indirectly, consensually best from right to left. Direct pupillary reaction best on right. *Fundi*: O.D., disc slightly injected but lamina cribrosa sharp in a pale shallow optic cup of moderate width. Vascular condition good; macular region and peripheral fundus clear. O.S., disc very pale, margins sharp; lamina cribrosa clearly outlined in a shallow, wide, glistening optic cup. Fundus otherwise as in O.D. *Fields* (fig. 34) show a condition on the left approaching Stage VII and on the right a typical though advanced Stage IV, with considerable macular involvement. V.O.S. $\frac{2}{200}$, V.O.D. $\frac{20}{200}$.

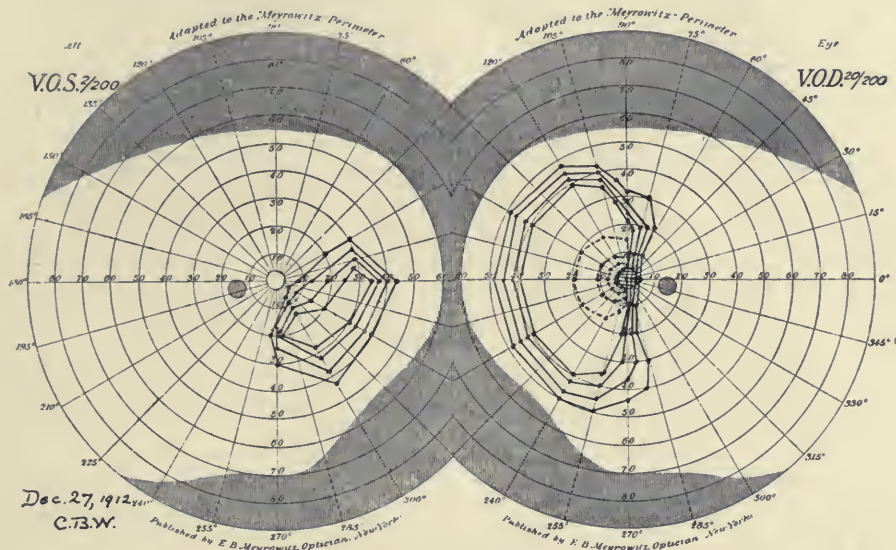


FIG. 34.—Case 9. Fields of December 27, 1912, before operation.
O.S. approximating Stage VII; O.D. in an advanced Stage IV.

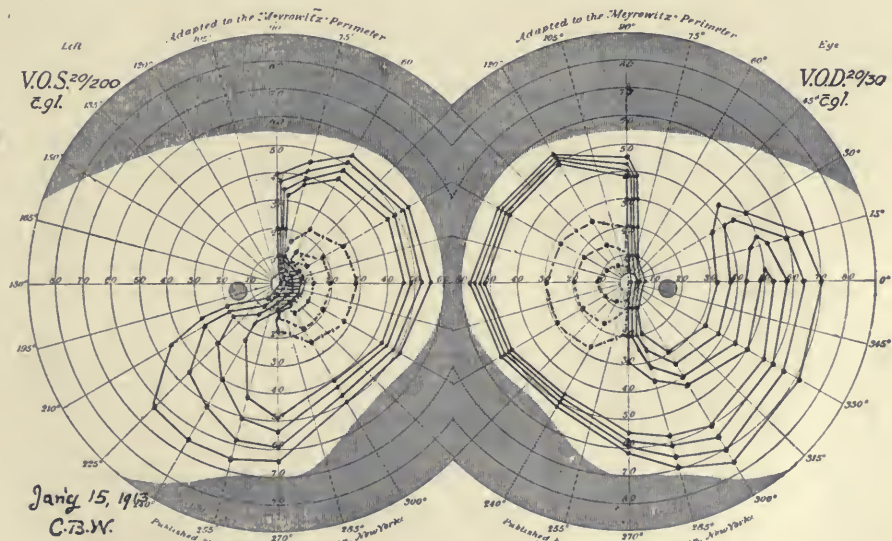


FIG. 35.—Case 9. Fields of January 15, 1913, four days after operation, showing recession to a full Stage III on the right, and on the left an astonishing change from Stage VII to one just short of Stage III.

January 11, 1913.—*Operation.* Usual transphenoidal procedure with partial extirpation of chromophobe struma. Uneventful recovery.

January 15 (Fourth day).—*Fields* show an astonishing improvement (fig. 35), particularly in the left eye, which has receded from Stage VII to an advanced Stage III. V.O.S. $\frac{20}{200}$, V.O.D. $\frac{20}{20}$.

January 19 (Eighth day).—*Fields* (fig. 36) and vision show further improvement. V.O.S. $\frac{20}{20}$, V.O.D. $\frac{20}{20}$.

January 23. (Twelfth day).—*Fields* (fig. 37) show an advance to Stage III on the left with increase in acuity from $\frac{20}{200}$ to $\frac{20}{20}$ in twelve days; on the right the form periphery has fused to the largest disc, and the vision has increased from $\frac{20}{200}$ to $\frac{20}{20}$ in the twelve days.

Patient discharged. No further report or reply to inquiry.

Comment.—It is regrettable that this patient has been lost sight of, for it would have been interesting to see whether a still further recession, possibly to Stage I or Stage II, did not occur in the left eye. It is presumable that nearly normal conditions may for a time have been regained in the right eye, where so far as acuity, outlines and duration of the process were concerned, the condition corresponded closely with that of the right eye in Case 6 already recorded and which fortunately could be followed through.

The following case report serves to show that even when Stage VIII has been reached, with blindness, one may still cling to the hope that a certain degree of useful vision may be restored, provided the implication of the nerves has not been of too long duration, and provided that a favourable condition such as a cyst is encountered.

Case 10 (J.H.H., Surg. No. 28,382).—*Cystic struma with hypopituitarism. Pronounced neighbourhood symptoms. Operation. Partial restoration of vision after blindness.*

September 13, 1911.—Admission of Mrs. E. J. W., aged 44, referred by Dr. D. B. Smith, of Setart, West Va. A characteristic case of hypopituitarism with adiposity, amenorrhœa, somnolence, &c. Complete absence of sellar outlines. Severe headaches began in 1909, but ceased after a year, when her vision began to fail, according to the history advancing as a bitemporal blindness. Since December of 1910 vision has been practically *nil*, though until three weeks before entrance she could distinguish moving objects. She states that vision faded first in the left eye and then in the right.

Examination of eyes.—Movements complete but slight exophoria. No nystagmus, ptosis or exophthalmos. Some divergence of globes. Pupils equal and moderately dilated. Right pupil reacts feebly to light, and there is bare perception of strong light; left pupil has sluggish indirect reaction. *Fundus*: O.U., optic disc pearly white; margins irregular but sharp and pigmented; lamina cribrosa sharply outlined; no œdema of the nerve-head.

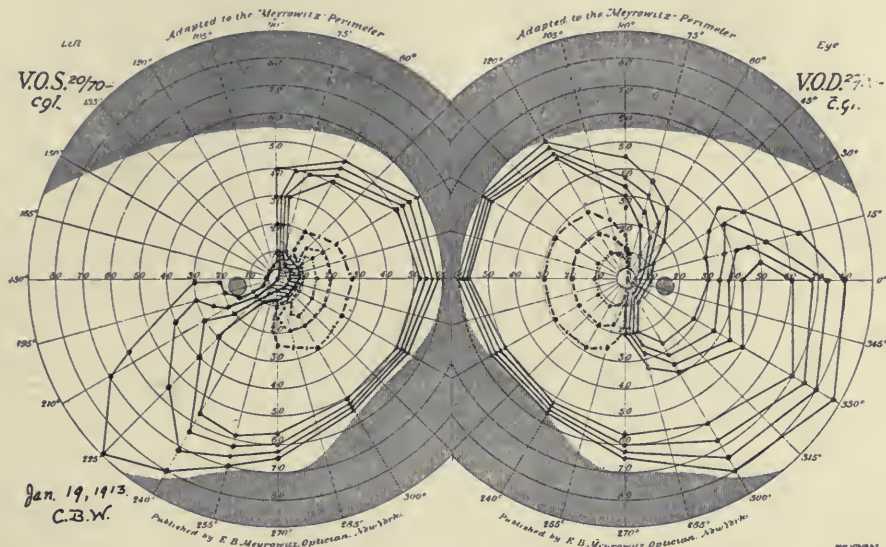


FIG. 36.—Case 9. Fields of January 19, 1913, eight days after operation, with further improvement.

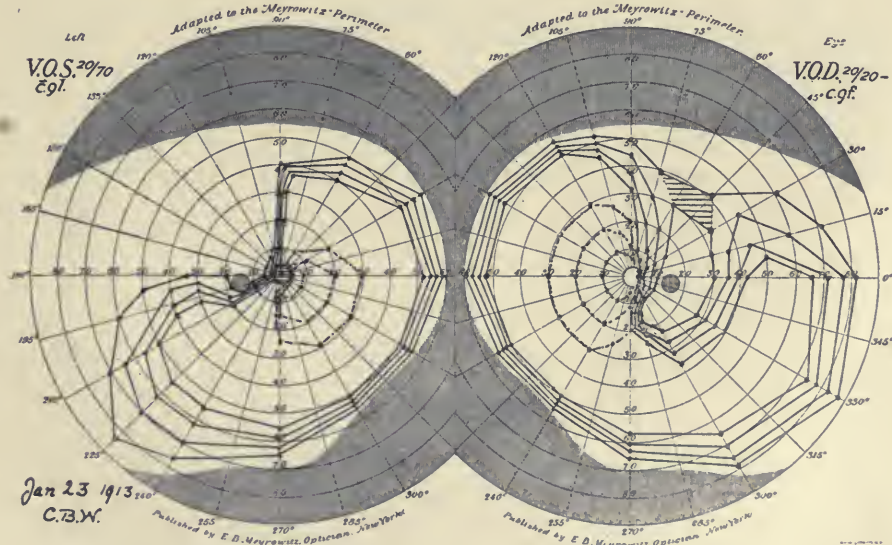


FIG. 37.—Case 9. Fields of January 23, 1913, twelve days after operation. Showing O.S., an advance to Stage III; O.D., a fusion of the peripheries of the larger disc.

Vessels and peripheral fundus show no change. *Fields*: Perimetry precluded. Faint light perception, limited to right temporal retina.

September 18.—Owing to a misinterpretation of the case and thinking it one of frontal lobe tumour, Dr. Sharpe performed a right exploratory osteoplastic craniotomy with a decompression. Her condition remained unaltered.

October 11.—*Operation.* Evacuation of cystic struma by transphenoidal approach. Patient could count fingers the afternoon of operation. No post-operative complications. Subjective improvement in vision continued. Perimetry was first employed on October, 17 1911.

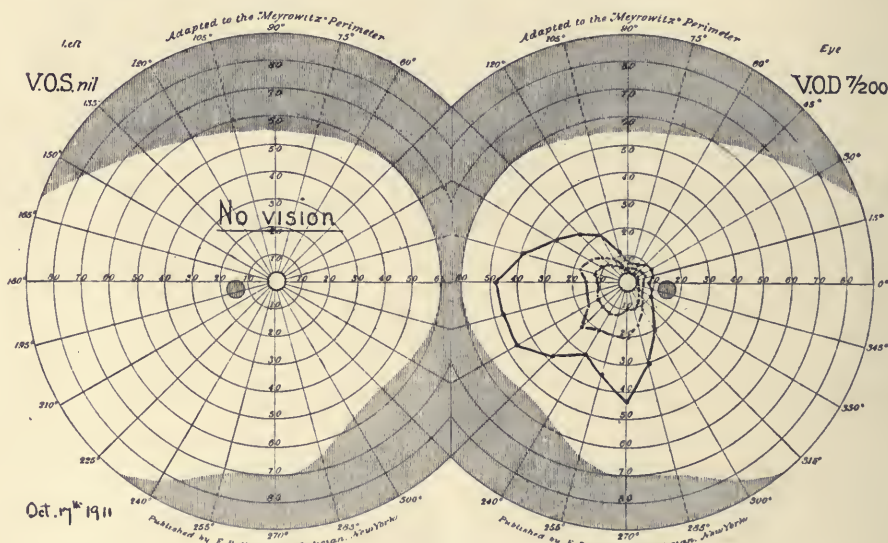


FIG. 38.—Case 10. Fields of October 17, 1911, with 0.5 cm. discs six days after operation. Pre-operative vision *nil*.

October 17.—*Fields* (fig. 38) show the restoration of something more than a quadrant of lower nasal vision with the macula included in the field in the right eye. V.O.S. *nil*, V.O.D. $\frac{7}{200}$.

October 30.—*Fields.* No change in outline. V.O.D. $\frac{15}{200}$.

November 6 and November 16.—*Fields* show no change. V.O.D. $\frac{15}{200}$. Discharged.

March 6, 1912.—By letter. Vision remains the same. General condition much improved.

Comment.—In this patient the condition in the least affected eye, the one in which vision returned, had advanced to a point at which shadows were no longer perceptible and fields could not be charted, in fact almost to Stage VIII.

It is one of the older cases and unquestionably from what we now know more careful perimetry would have shown a relative central scotoma, and it is possible too that fixation was not accurate and that the plotted area should have been registered farther to the nasal side.

There are several other cases in the series in which a modicum of vision has slowly returned in an absolutely blind eye. Indeed in one of the patients in the homonymous group, a woman who was completely blind before operation, some vision returned in both eyes. In only one other case in the series, in addition to this Case 10, was the return of vision after blindness accompanied by a return of colour perception as well as of perception for form.¹

When, in these blind patients, despite the widened pupil some reaction to light is still retained the prognosis for some restoration of vision is naturally better than when the pupillary reflex is lost, for it implies that there are still some functionally intact fibres. We have seen, however, by the return of a patch of vision in the left eye in Case 5, which had been blind for a year before the operation, and in which the direct light reflex was completely abolished, that some light perception may be regained even under these more unpromising conditions.

Bizarre types of field distortion.—The foregoing ten cases have been selected as fairly representative, at the time of admission, of the stages into which we have divided hemianopsia. Attention may again be called to the fact that they all represent examples of pituitary disease (acromegaly, or its reverse clinical state) in which the sella has been widely distended by a tumefaction or so-called struma of the gland itself. Such a lesion in the course of its enlargement naturally presses upon the chiasm from below and behind, affecting the various fasciculi of the nerve in fairly definite progression.

It must be realized, however, as has been already emphasized, that when the gland is subject to a marked enlargement or tumefaction it is capable of bursting through the dural capsule with ultimate extensive invasion of the intracranial chamber. Even under these circumstances the nerves may entirely escape from functional pressure implication, for they are capable of extreme anatomical distortion without demonstrable perimetric change. Still, when the growth has extended through the dural envelope and made its way upward it may envelop

¹ This other case was recorded as Case 22 in "The Pituitary Body and its Disorders," 1911. Blindness had been complete for only two days, and there was sufficient return of vision in each eye to permit of perimetry.

the chiasm and its four branches in irregular ways and produce bizarre types of field deformation which deviate from the regulation stages which we have heretofore described.

In the following case, for example, the dorsal uncrossed fasciculi became involved before the ventral fasciculi, leaving a fairly clear-cut superior nasal quadrantal field of preserved vision, and the tendency toward restoration appeared in the upper nasal field rather than in the lower, as is the rule.

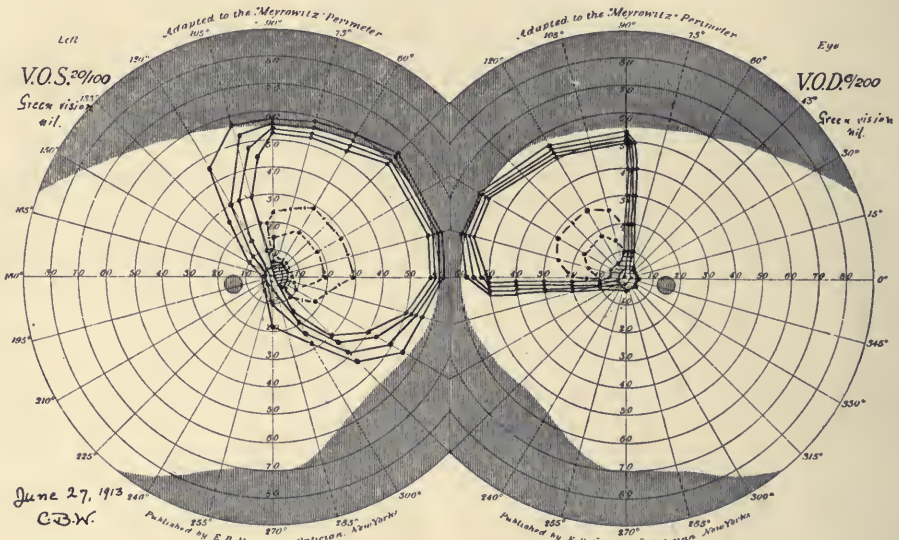


FIG. 39.—Case 11. Fields of June 27, 1913, three weeks before operation, showing unusual though fairly symmetrical type of bitemporal defect.

Case 11 (P.B.B.H., Surg. No. 203).—Struma with hypopituitarism and unusual field deformation.

June 27, 1913.—Admission of Morris B., aged 43, a storekeeper, referred by Drs. W. Simon and Charles H. May, of New York. A fairly typical example of hypophysial insufficiency, with drowsiness, headaches and loss of vision as the chief complaint. Lowering of vision first noticed three years ago, with progressive advance. Diplopia, present for one year, has now disappeared. A greatly enlarged sella with absorbed dorsum.

Examination of eyes.—Pupils small, equal; sluggish reactions. Hemipic reaction in both eyes, best seen on the left. No apparent oculomotor palsies. *Fundus*: marked pallor of discs with crescentic pigment deposit; veins full and tortuous. Optic cup filled with new tissue; lamina cribrosa obscured. No cedema or measurable swelling. *Fields* (fig. 39) show a fairly symmetrical

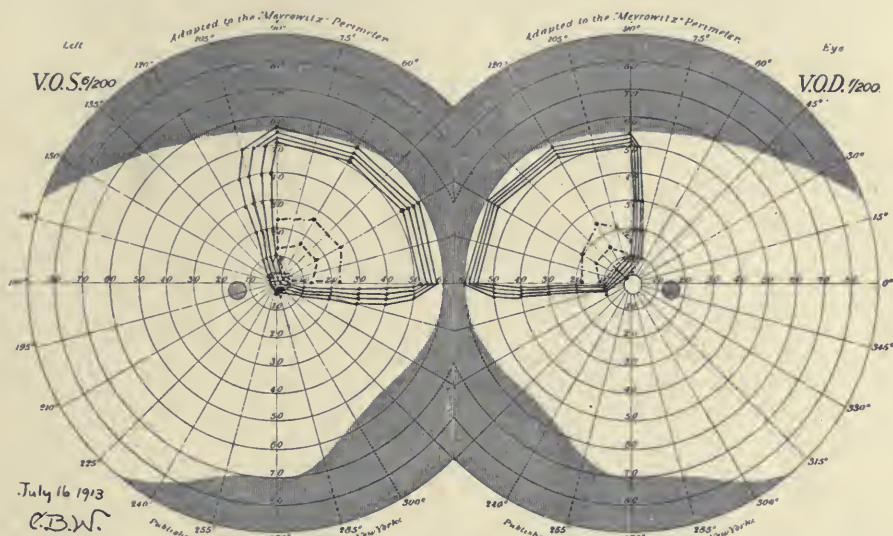


FIG. 40.—Case 11. Fields of July 16, 1913, three days before operation, showing further advance in untreated lesion.

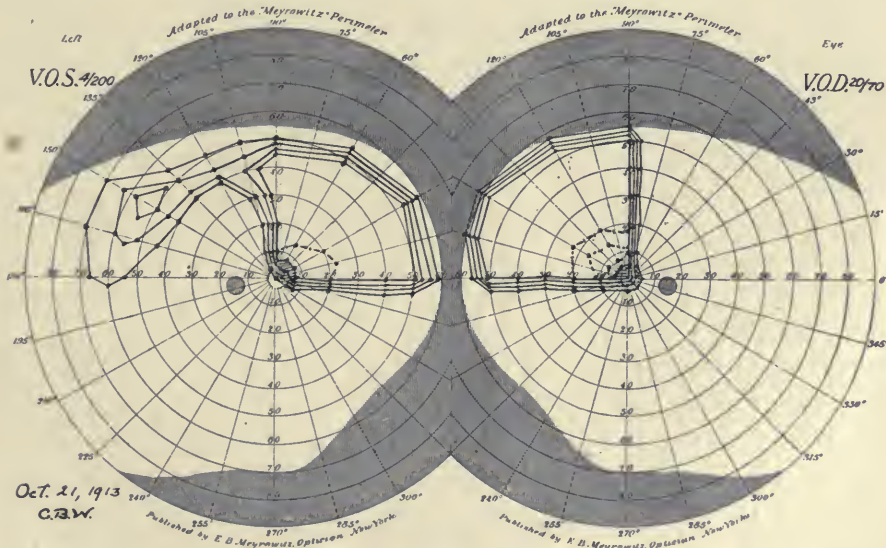


FIG. 41.—Case 11. Fields of October 21, 1913, showing O.S. tendency toward upper temporal field restoration.

preservation of vision in the upper nasal quadrants, with enfeeblement of the macular bundle on each side. V.O.S. $\frac{20}{100}$, V.O.D. $\frac{6}{200}$.

Operation advised and deferred.

July 15.—*Readmission*. Condition advanced. *Fields* (fig. 40) now limited to the quadrants and show more extensive macular impairment. V.O.S. $\frac{6}{200}$, V.O.D. $\frac{1}{200}$.

July 19.—*Operation*. Usual transphenoidal procedure with partial extirpation of characteristic chromophobe struma. Uneventful convalescence.

July 24.—*Fields* unchanged. Some subjective improvement in vision.

August 2.—*Fields* unchanged. Improvement in vision on the right. V.O.S. $\frac{4}{200}$, V.O.D. $\frac{15}{200}$. *Discharged*.

October 21.—*Reports for examination*. *Fields* (fig. 41) to larger discs have shot out over left upper temporal quadrant, but there is no central visual improvement in this eye, unlike the other, where the outline remains unaffected. V.O.S. $\frac{4}{200}$, V.O.D. $\frac{20}{70}$.

Comment.—The secondary changes in the fundi, the presence of diplopia, as well as the unusual field defects, make it evident that the lesion had extended upward and around the nerves. Hence our operation did not offer much chance of improvement. The way in which the field peripheries, according to the last post-operative observation, have spread out on to the left temporal field resembles, though upside-down, the manner of restoration which occurs in the standard type of recession towards Stage III.

Many other examples of irregular fields might be cited from this group of primary intrasellar enlargements in which the nerves have become involved by an upward extension of a primarily intrasellar lesion, but this single case may perhaps suffice.

One thing further may deserve a word of mention in connexion with these cases, and that is the not infrequent combination of a normal with a blind eye, of which condition there are three or four illustrative cases in the series, not to mention a few others in which the field of the seeing eye has begun to show an early slant (Stage I) of the upper temporal periphery. It is difficult, of course, in these cases, without a definite history of the way in which the field of the blind eye first became involved, and without waiting for changes in the seeing eye, to tell whether the case really belongs in the homonymous or bitemporal group. Unless associated with a congenital absence of chiasmal crossing, which is rare, the condition of course must indicate an implication of a single optic nerve anterior to the chiasm, for otherwise the temporal field in the seeing eye would necessarily have shown constriction.

(b) *The suprasellar tumours causing bitemporal hemianopsia.*—

We come now to a group of cases in which the chiasmal involvement is due to a lesion of quite a different nature—namely, to a superimposed (rather than an intrasellar) tumefaction, the most characteristic example of which, the *Hypophysenengangtumor* of Erdheim, is usually a cystic growth of pharyngeal anlage situated in the interpeduncular space, where it often surmounts a sella which gives fairly normal outlines to the X-ray. On first thought one would assume that in these cases the perimetric defect would first appear in the lower temporal field, but this we have not found to be the case. Indeed, our few most striking examples of defects starting in the lower quadrants have occurred in conjunction with large primarily intrasellar strumas.

In this group of patients with superimposed tumours there occur many illustrations of field defects which correspond in all respects with the typical stages, examples of which have already been given. From a surgical standpoint, however, these cases are far less favourable than the others, and consequently there have been fewer notable instances of post-operative improvement in perimetric conditions. Moreover, as a rule, the condition is a slowly progressive one, without particular discomforts, and therefore is often neglected, so that in many of the patients one or both eyes at the time of admission have advanced well beyond Stage IV. As is true also of the group we have just considered, so in these cases the process by no means advances with bilateral symmetry, for though the stages occur in characteristic sequence one eye is usually well in advance of the other.

One or two examples may be given. The first illustrates a satisfactory ultimate post-operative recession in each eye from Stage IV to approximately Stage I.

Case 12 (J.H.H., Surg. No. 28,986).—Hypopituitarism with interpeduncular cyst. Operation. Meningitis. Restoration of vision.

December 26, 1911.—Admission of James A., aged 19, a student, referred by Drs. Walker and Jelliffe, of New York. An example of hypophysial insufficiency of the puerile type, with somewhat enlarged and distorted sella showing a suprasellar shadow. Severe headaches for four or five years, aural pain with tinnitus, &c. The hemianopsia was not detected until the present year, though vision began to fail in 1909, first in the right and then in the left eye. Rapid advance of late.

Examination of eyes.—Pupils equal; normal reactions to light and accommodation; hemianopic pupillary reaction present. *Fundi*: Pallor of both discs, with sharp pigmented margins; considerable new tissue with obscuration of physiological cup and lamina cribrosa; disc elevated 2 D. with

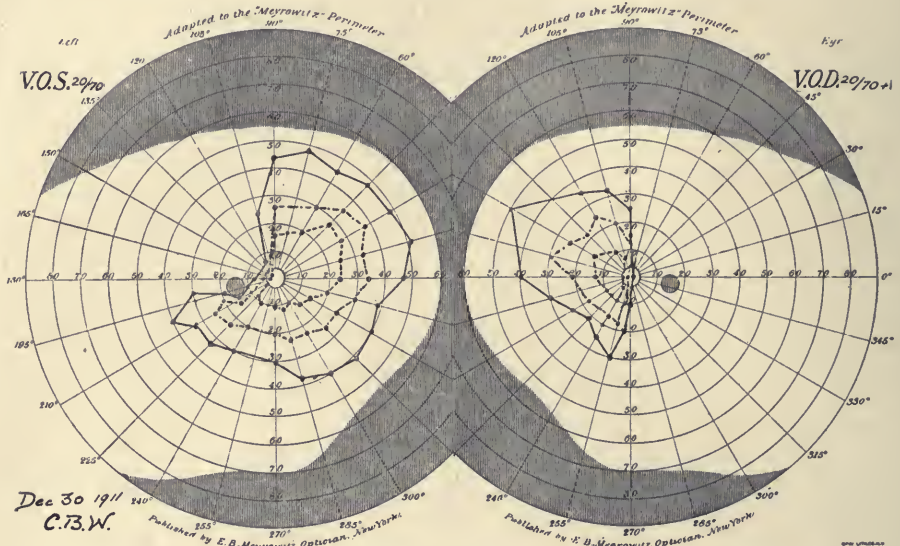


FIG. 42.—Case 12. Fields of December 30, 1911, four days before operation. O.S., Stage III; O.D., Stage IV. Constriction possibly due to associated low grade papilloedema.

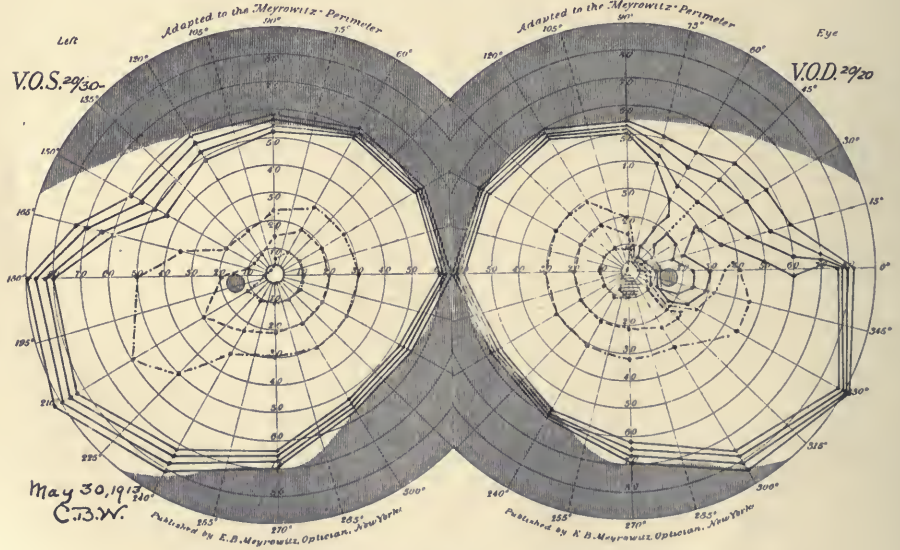


FIG. 43.—Case 12. Fields of May 30, 1913, sixteen months after operation, showing final recession of the process approximately to Stage I.

hyperopic astigmatism. *Fields*, December 26 and 30 (fig. 42) show Stage III approaching Stage IV on the left, and Stage IV on the right. V.O.S. $\frac{2}{7}$ °, V.O.D. $\frac{2}{7}$ ° +.

January 4, 1912.—Operation. Attempted transphenoidal procedure, abandoned owing to anatomical peculiarities necessitating further X-ray studies.

January 10.—Second operation. Re-entry by former route; evacuation of large cyst after cerebrospinal space had been opened. Immediate great improvement in vision, but a cerebrospinal rhinorrhœa became established and after a few days, before perimetry was used, there occurred a sharp attack of cerebrospinal meningitis, from which there was a final recovery.

Fields taken on *January 31, February 3 and 5* (bedside perimetry) and on *February 15 and 26*, show a progressive improvement, particularly in the left eye, the temporal hemianopsia on the right persisting. Patient discharged.

He was subsequently seen and examined on several occasions, no further change in the fields being observed, but as there was some recrudescence of headaches and some continued hyperæmia of the discs on *April 29* a sub-temporal decompression was performed.

May 30, 1913.—Reports for examination. Has been completely free from discomforts since the decompression. His vision has also greatly improved. *Fields* (fig. 43) show a recession to Stage I, the right being somewhat behind the other.

Comment.—The first fields were taken before we came to use our more refined methods, and, on the left, serial discs would probably have shown wider peripheries. Moreover, in view of the lowered vision to $\frac{2}{7}$ °, there was probably a relative central haziness which our methods of three years ago did not detect or record. Doubtless the further story was considerably complicated by the meningitis which occurred, and unjustifiable risks—then hardly appreciated—were assumed in attacking a lesion of this kind from below. The final recession of the process to about Stage I in both eyes must have taken place slowly after the patient's recovery from the infection and his discharge from the hospital, and we have no records of the intervening stages. It is known that such recessions may take place spontaneously without operation—a matter to be touched upon later.

The following history shows that in cases of this kind the advancing field deformations may not conform to the typical stages which we have described. As in the foregoing, here also the condition was possibly complicated by a superimposed secondary atrophy.

Case 13 (P.B.B.H., Surg. No. 235).—Hypopituitarism with congenital suprasellar cystic tumour. Transfrontal operation. Fatality.

July 11, 1913.—Transfer of Dora A., aged 14, from Dr. Christian's medical

service. A small, undeveloped and undersized child, a previous inmate of many hospitals and the victim of many diagnostic errors—"diabetes insipidus," "constipation and obesity," "infantilism," "progressive emaciation," "cerebellar tumour," "tuberculosis," &c.

Formerly a very fat child, she has progressively become emaciated since 1910. For some years there have been headaches with vomiting, polyuria and polydipsia and disturbance of vision. She was brought to the hospital in a semi-conscious condition, from which she slowly emerged as a bright and attractive child. An X-ray shows the shadow of a suprasellar tumour [16] above a pituitary fossa of fairly normal outline.

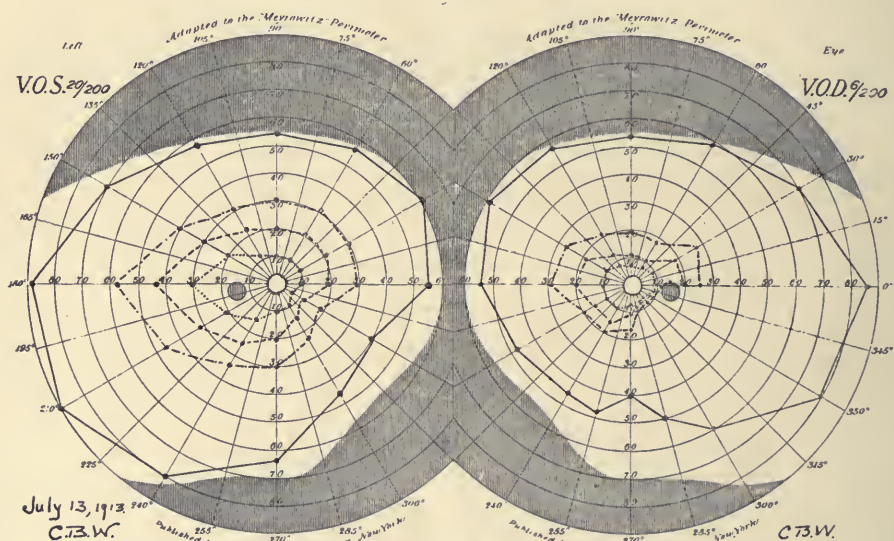


FIG. 44.—Case 13. Fields of July 13, 1913, plotted for $\frac{1}{4}$ sq. cm. disc only. Showing insignificant deformations on the first admission.

Disturbances of vision recognized for several years. Many attempts to correct by glasses. Diagnosis of "low grade optic neuritis" made in May, 1911. No history of diplopia.

Examination of eyes.—Pupils unequal, left larger than right. Reactions normal. Myopic astigmatism. *Fundi*: Discs pale and glistening. Lamina cribrosa obscured, optic cup obliterated, and some new tissue formation along the vessels, which are small. Marginal pigment upheaval. Optic atrophy, suggestive of previous optic neuritis. *Fields* (fig. 44) for normal $\frac{1}{4}$ sq. cm. discs only, show no especial constriction but an unchartable central scotoma on the right. V.O.S. $\frac{20}{200}$, V.O.D. $\frac{6}{20}$ (uncorrected).

July 16.—Operation. Right subtemporal decompression revealing a tense and wet brain. Subsequent to this operation there was complete freedom

from the former headaches. The fields of August 16 showed no further change. Discharged.

August 22.—*Reports for examination.* Fields (fig. 45), plotted with normal $\frac{1}{4}$ sq. cm. discs only show a marked advance in the constriction with especial implication of macular areas. V.O.S. $\frac{20}{200}$, V.O.D. $\frac{5}{200}$.

September 22.—*Readmission.* Return of pressure symptoms. Decompression area tense. Fields: September 29 (fig. 46), plotted for normal $\frac{1}{4}$ sq. cm. discs alone, show further advance. V.O.S. $\frac{10}{200}$, V.O.D. $\frac{1}{200}$ (uncorrected).

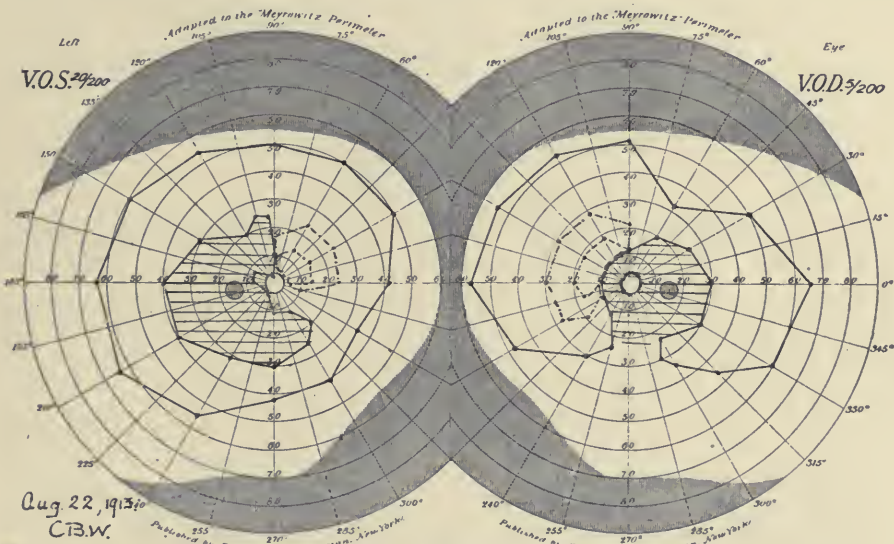


FIG. 45.—Case 13. Fields of August 22, 1913; plotted for $\frac{1}{4}$ sq. cm. discs only. Showing marked advance in five weeks with chief loss in paracentral areas.

October 21.—Periods of intense pressure symptoms have alternated with more comfortable periods, but vision has been failing rapidly. Fields (fig. 47) show progressive irregular advance. A small area of preserved central vision permits fixation, so that perimetry is still possible. V.O.S. $\frac{10}{200}$, V.O.D. $\frac{1}{200}$ (uncorrected).¹

November 4.—Further loss of vision. Fields about as at last note.

¹ Some discrepancies may be observed in the charts for the case due to the fact that perimetry was particularly difficult owing to the child's inattention from drowsiness and asthenia. Thus in the right eye on August 22 (fig. 45), there was in all probability a bridge of vision enclosing the paracentral scotoma, for this was still demonstrable on the test of September 29 (fig. 46). Fortunately up to the last test sufficient macular vision was preserved to make central fixation possible, but the employment of serial discs was precluded owing to the ease with which the child became fatigued.

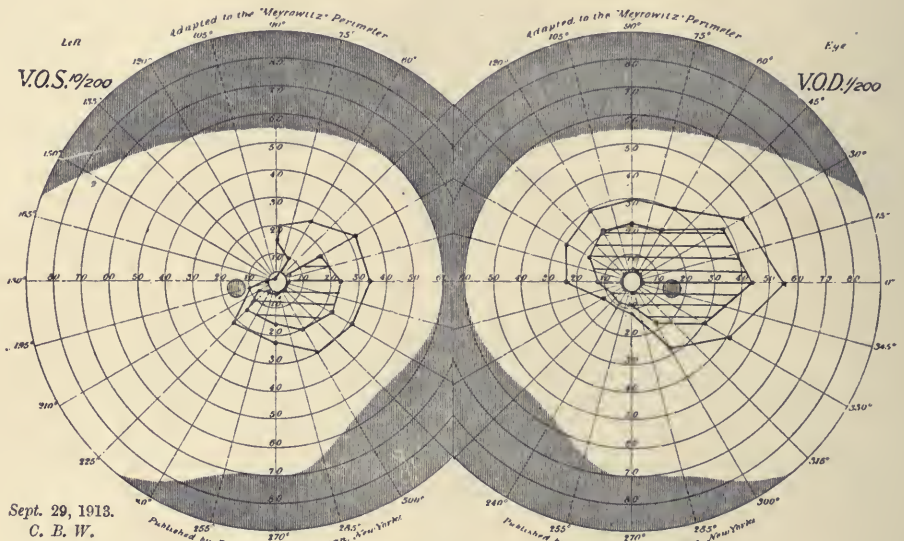


FIG. 46.—Case 14. Fields of September 29, 1913; plotted for $\frac{1}{2}$ sq. cm. discs only, showing further rapid progress, but with retention of macular fibres permitting of central fixation.

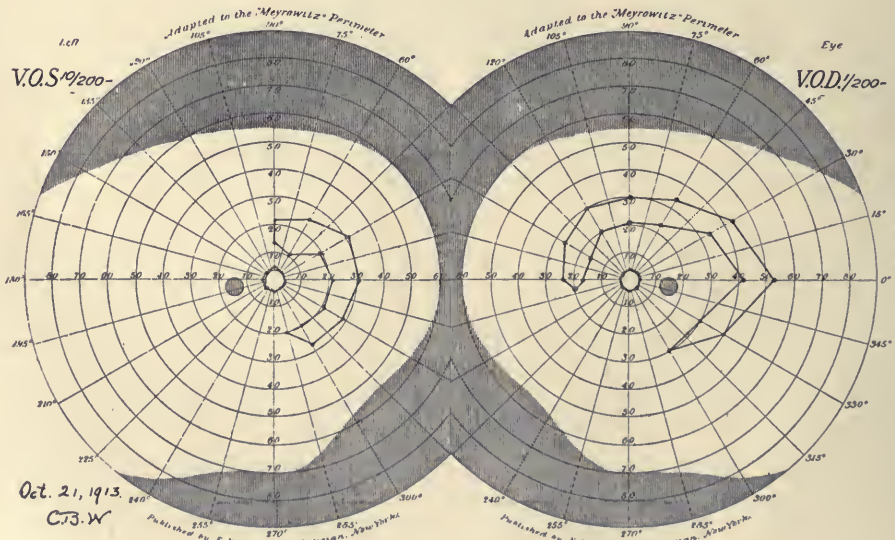


FIG. 47.—Case 14. Last fields of October 21, 1913, to $\frac{1}{2}$ sq. cm. discs, showing conditions before fatal operation. Fixation permissible owing to retained central vision.

November 17.—Operation. Transfrontal procedure with disclosure of irregular calcareous tumour, wrapped around chiasm. Attempt to dislodge the tumour caused bleeding. Post-operative hyperthermia. No return of consciousness.

November 21.—Second-stage operation. Transfrontal removal, with no anæsthesia, of large interpeduncular growth, causing unavoidable damage to interpeduncular tissues and death after twenty-seven hours.

Comment.—In this case, without the X-ray disclosure of a tumour, we should in all likelihood have been as uncertain of the diagnosis as our various predecessors have been.

It is notable that almost invariably in these cases of pituitary tumour (e.g., in all but one of the thirteen here recorded), even though pressure symptoms are pronounced, a swelling of the nerve-head does not occur. This we have attributed to the fact that the sheath of Schwalbe is so blocked as to prevent the crowding down of cerebro-spinal fluid around the nerve—in other words, to an interference with the physical conditions under which a choked disc is produced.

However, in a number of the cases in the series—of which Case 12 and Case 13 are examples—a low grade of œdema, occasionally with new tissue formation, has become superimposed on a primary atrophy, when intracranial pressure has become extreme and the nerve-sheaths have not been occluded by the growth. Usually, as in this particular patient, the choked disc is secondary to an internal hydrocephalus.

The so-called primary optic atrophy.—The comment on the foregoing case naturally brings up the question of a primary versus a secondary atrophy; and just how far the secondary changes may have been responsible for the irregular field deformations may be a matter of opinion. We have seen other examples of bizarre fields, most of them similarly associated with a normal sella and a congenital tumour, in which normal peripheries have been restored after a successful operation—in one case, indeed, after the constriction had advanced as far as in the last fields of this Case 13. In none of the cases in which prompt post-operative improvement occurred did the so-called primary atrophy show evidence of a superimposed œdema with its secondary new tissue formation.

We are aware that exception may be taken to our designation of the conditions of the nerve-head which we have observed, as “primary optic atrophy,” for the reason that the subsequent return of vision in many of the cases disproves the presence of atrophy, on a strict

construction of the term. However, many of the patients have come to us after ophthalmologists elsewhere have given a similar pronouncement. Doubtless if left to itself the condition in every case would tend in the long run, despite the occasional spontaneous recessions of which the process is capable and to which many have called attention [10], toward a terminal and permanent blindness. In a few of our own cases the history records periods of lowered visual acuity and contracted field peripheries from which there has been a temporary recovery, though after an interval vision has again failed. This of course means that the growth is capable of periods of increased tension for one cause or another (œdema, vascularity, &c.), just as a thyroid struma may enlarge and subside, though the tendency lies in the direction of a final increase in size despite the fluctuations.

Undoubtedly there may be other conditions which may cause a similar glistening pallor of the nerve-head, such as the toxic amblyopias from tobacco, lead, illuminating gas and so on, but we feel, in view of the far greater frequency of this appearance from a mechanical pressure against the nerves and chiasm, that doubt should always be put upon the toxic explanation of the process until a hypophysial source of the atrophy has been excluded. The diagnosis of lead, tobacco, and of syphilitic amblyopia had previously been made in several of the cases in our series, subsequently proved to be hypophysial.

It is often impossible to tell from the appearance of the disc whether or not there has been an irrecoverable destruction of the nerve. As mentioned in the comment on Case 9, dependence must usually be placed on the preservation of pupillary reactions and on the retention of some light perception, no matter how dim. We have seen vision return in blind eyes, though only once or twice in eyes with completely lost pupillary reactions.

This all goes to show what one of us has emphasized before, that demonstrable perimetric defects are more an evidence of a physiological block than of an anatomical destruction of the nerves in view of the great degree of recoverability in the transmission of light impulses on the release of the nerves from pressure. This is further supported by the fact that in several cases the histological examination of nerves has shown but a scattering of degenerated fibres, even though the ophthalmoscope had previously demonstrated the characteristic pallor attributed to advanced atrophy and the perimeter an advanced field defect. No correspondence has been found to exist between sharply cut quadrantal or hemianopic field defects and patches of degeneration seen on cross section of the optic nerves, such degeneration as might be

expected in accordance with Henschen's diagrams; for we have found that clean-cut functional defects in the fields may occur without any equally clean-cut fascicular disposition of degenerated fibres in the nerves.¹

RECAPITULATION.

In a series of 454 cases classified as tumour of the brain there have been 101 in which the lesion was of hypophysial or parhypophysial origin, and in 81 of these cases chiasmal involvement led to deformations of the fields of vision. These deformations tended at the time of admission to be bitemporal in 26 cases, homonymous in 12, were unclassifiable in 8 cases, and the remaining 35 showed blindness in one or both eyes, making it difficult to tell in which group—bitemporal or homonymous—they belonged.

In cases of bitemporal hemianopsia it is unusual for the field defects to be bilaterally symmetrical, the text-book representation of the condition, with a vertical meridian dividing blind from seeing retina in each eye, being relatively uncommon.

In the majority of cases, whether of intra- or suprasellar tumour, the first perimetric indication of the process is shown by a slant in the boundary of an upper temporal form field and a corresponding quadrantal defect in the colour peripheries. For clinical convenience this is designated as Stage I of the process, and with a progressive lesion the field defects advance in characteristic fashion through Stage IV of actual hemianopsia to Stage VIII when blindness has ensued. In all stages the loss of colour perception is usually in advance of that for form, and the condition in one eye is usually in advance of that in the other, so that every possible stage combination in the two eyes may be met with.

When relief from pressure has been afforded by operative measures the recession of the defects takes place in a sequence, the reverse of that characterizing the stages of an advancing process. In the receding process relative paracentral scotomata often persist, as the functional vulnerability of the macular and paramacular fibres appear to be greater than that of the other fasciculi. Restoration of normal field peripheries is possible even when the process has advanced to or beyond the Stage IV of typical half vision, and some vision may be regained even after blindness has occurred, provided it has not been of too long duration.

In view of the prompt restorations in field outlines which may follow operative relief from pressure, it is evident that the so-called primary optic atrophy often does not represent an actual anatomical

¹ This matter will be made the special subject for further communication.

degeneration so much as a physiological block to the transmission of visual impulses.

In conclusion.—Detailed perimetry with small test objects of serial sizes, particular attention being paid to the shading off of the upper temporal peripheries and to the presence of relative paracentral scotomata in the same quadrant, is advocated for patients with pituitary disease in order that stages of hemianopsia antecedent to those usually recognized may be detected.

BIBLIOGRAPHY.

- [1] BARKER, L. F. "The Nervous System and its Constituent Neurones," New York, 1899, pp. 782 *et seq.*
- [2] BJERRUM. "Om en Tilføjelse til den sad. vaulige Synsfelt undersogelse samt om Synsfeltet ved Glaucom," *Nord. Ophthal. Tidsskrift*, 1889, vol. ii, p. 141.
- [3] *Idem.* "Om Glaucomets klinische Afgræning," *Nord. Ophthal. Tidsskrift*, 1892, vol. v, pp. 71, 129.
- [4] *Idem.* "Ueber eine Zufügung zur gewöhnlichen Gesichtsfeldmessung und über das Gesichtsfeld beim Glaukom," *Trans. X Internat. Med. Cong.*, Berlin, 1890, Abth. x, S. 66-79.
- [5] BOGATSCH. "Beitrag zur Ätiologie der bitemporalen Hemianopsie mit besonderer Berücksichtigung der Hypophysiserkrankungen," *Klin. Monatsbl. f. Augenheilk.*, 1912, N.F., Bd. xiv, S. 313-325.
- [6] CUSHING. "The Pituitary Body and its Disorders," New York, 1912, Case xviii, p. 108.
- [7] CUSHING and HEUER. "Distortions of the Visual Fields in Cases of Brain Tumour," *Bull. of Johns Hopkins Hosp.*, 1911, vol. xxii, pp. 190-195.
- [8] *Idem.* "Distortions of the Visual Fields in Cases of Brain Tumour," *Journ. Amer. Med. Assoc.*, 1911, vol. lvii, pp. 200-208.
- [9] CUSHING and WALKER. "Distortions of the Visual Fields in Cases of Brain Tumour, Binasal Hemianopsia," *Arch. Ophthal.*, New York, 1912, vol. xli, pp. 559-598.
- [10] DE SCHWEINITZ. "Some Remarks on the Ocular Symptoms of Pituitary Disease, &c.," *Penn. Med. Journ.*, 1911-12, vol. xv, pp. 515-529.
- [11] DE SCHWEINITZ and CARPENTER. "The Ocular Symptoms of Lesions of the Optic Chiasm, with the Report of Three Cases of Bitemporal Hemianopsia," *Journ. Amer. Med. Assoc.*, 1905, vol. xlv, p. 81.
- [12] DE SCHWEINITZ and HALLOWAY. "A Clinical Communication on Certain Visual-field Defects in Hypophysis Disease, with Special Reference to Scotomas," *Journ. Amer. Med. Assoc.*, 1912, vol. lix, pp. 1041-1045.
- [13] FISHER, J. HERBERT. "Discussion on Diseases of the Pituitary Body," *Proc. Roy. Soc. Med.*, 1913, vol. vi, Neur. and Ophthal. Sect., pp. liii-lxviii.
- [14] *Idem.* "The Pituitary Body and Lesions of the Optic Chiasm," *Trans. Ophthal. Soc. U.K.*, 1911, vol. xxxi, pp. 51-93.
- [15] HENSCHEN. "Klinische und anatomische Beiträge zur Pathologie des Gehirns," Upsala, 1892, Zweites Heft, S. 217.
- [16] LUGER, ALFRED. "Zur Kenntnis der im Röntgenbild sichtbaren Hirntumoren mit besonderer Berücksichtigung der Hypophysenhangeschwulste," *Fort. a. d. Geb. d. Röntgenstrahlen*, 1914, Bd. xxi, S. 605.
- [17] RÖNNE. "Gesichtsfeldstudien über das Verhältnis zwischen der peripheren Sehschärfe und dem Farbensinn, speziell die Bedeutung derselben für die Prognose der Sehnervenatrophie," *Klin. Monatsbl. f. Augenheilk.*, 1911, N.F., Bd. xi, S. 154.
- [18] *Idem.* "Ueber den Fasernverlauf im Chiasma, beleuchtet durch einige Gesichtsfelduntersuchungen," *Klin. Monatsbl. f. Augenheilk.*, 1910, N.F., Bd. x, S. 455.
- [19] *Idem.* "Ueber das Gesichtsfeld beim Glaukom," *Klin. Monatsbl. f. Augenheilk.*, 1909, N.F., Bd. vii, S. 12.
- [20] WALKER, C. B. "New Instruments for Perimetry," *Arch. Ophth.*, 1913, vol. xlii, p. 577.

THE DEMONSTRATION OF *SPIROCHÆTA PALLIDA* IN
CHRONIC PARENCHYMATOUS ENCEPHALITIS (DE-
MENTIA PARALYTICA).

BY JAMES McINTOSH, M.D. ABERD.

Beit Memorial Research Fellow; Late Research Scholar of the Grocers' Company.

AND

PAUL FILDES, M.B., B.C. CANTAB.

Assistant Bacteriologist to the London Hospital.

(From the Bacteriological Laboratory of the London Hospital, Professor
William Bulloch, F.R.S.).

IN a previous issue of BRAIN [1] we discussed the relation of dementia paralytica to syphilis, and described how Noguchi and others had succeeded in demonstrating *Spirochæta pallida* in the brains of such cases. We mentioned that we ourselves had confirmed these findings, and since, so far as we are aware, there has been no detailed publication on the subject in this country, we now give illustrations of the cases referred to by us.

THE TECHNIQUE OF EXAMINATION.

The brains or fragments of brain were examined fresh, as received by post from Dr. Gettings, of the Wakefield Asylum, by the method of dark-ground illumination. The most satisfactory illuminator is the parabolic condenser of Zeiss, associated with a $\frac{1}{6}$ in. objective (correction collar), and a No. 6 compensating eyepiece. The best source of light is a small arc lamp the rays of which are passed through a spherical condenser filled with water. A small fragment of cortical grey matter about the size of a pin's head is removed from the specimen and broken up in a drop of saline in a watch-glass. The tissue should not be thoroughly emulsified since the specimen will then be too opaque for satisfactory examination. A small quantity of the fluid is placed on a slide and examined.

After five or ten minutes if the examination is negative a new area of the cortex should be taken, and thus a large area of the brain may be investigated. Wherever spirochætes were found that portion

of the brain was fixed in formalin and stained by Noguchi's modification of Levaditi's method for demonstrating spirochætes in sections. It is clear that the dark-ground technique gives no information as to the relation of the organisms to the surrounding tissues, but it very much facilitates the examination of sections, and almost ensures that spirochætes are present in the fragment selected.

The detection of *Spirochæta pallida* in sections of the brain is sometimes easy, but often extremely difficult. As will be seen from the accompanying exact drawings the organisms are at times degenerate or atypical, and if such an example is met with in a specimen in which the nerve fibrils have also taken up the silver, it is quite impossible to be certain that the object is a spirochæte. It is only when areas are found in which the fibrils are unstained, or when a focus contains typical as well as atypical spirochætes, that the diagnosis may be made with confidence.

We have therefore found that it is preferable to traverse a section all over rapidly, rather than to try to disclose single spirochætes in unfavourable areas. If this method is adopted, it will usually happen that a focus may be found in one portion of the slide only, and the spirochætes may be so numerous in this focus that they could not be overlooked. It is unusual to find a single spirochæte which is not accompanied by several others in the vicinity.

NOTES OF THE CASES.

The following details of the cases include short abstracts of the clinical notes communicated by Dr. Gettings:—

Case 1.—W. G., male, aged 30. Duration of symptoms unknown; admitted June 13, 1912, died January 4, 1914. Clinical manifestations of dementia paralytica; grandiose delusions, speech and hands tremulous, pupils dilated and unequal.

Autopsy.—Great excess of subdural fluid. Brain weighed 1,590 grm. Pia increased in vascularity, thickness and opacity; large arteries atheromatous, grey matter dark and congested, granulations in fourth ventricle.

Microscopic appearances.—Slight cellular infiltration of the pia-arachnoid; general perivascular infiltration of the vessels in the cortex and in the medulla. Plasma-cells are relatively few in the infiltrations, the majority being large mononuclear cells (endothelial). In some places there is a slight occlusion of the small vessels.

Spirochætes.

Dark ground	...	Spirochætes very rare, found only in the frontal region.
Sections	...	None found.

Case 2.—M. A. H., female, aged 46. Duration of mental symptoms indefinite, said to have had a stroke in June, 1911; admitted August 20, 1913, died January 9, 1914. Pupils equal and contracted; patient had no knowledge of her surroundings or of what was said to her.

Autopsy.—Brain weighed 1,180 gm. Great increase of subdural fluid. Pia thickened, opaque, and adherent. Grey matter slightly atrophic but reddish in appearance, marked granularity of floor of fourth ventricle.

Microscopic appearances.—Marked infiltration of the pia-arachnoid with plasma-cells and lymphocytes; vessels appear to be normal. In the brain there is only a moderate perivascular infiltration, but in a few places it is very marked. No evidence of glial proliferation, pyramidal cells slightly degenerate.

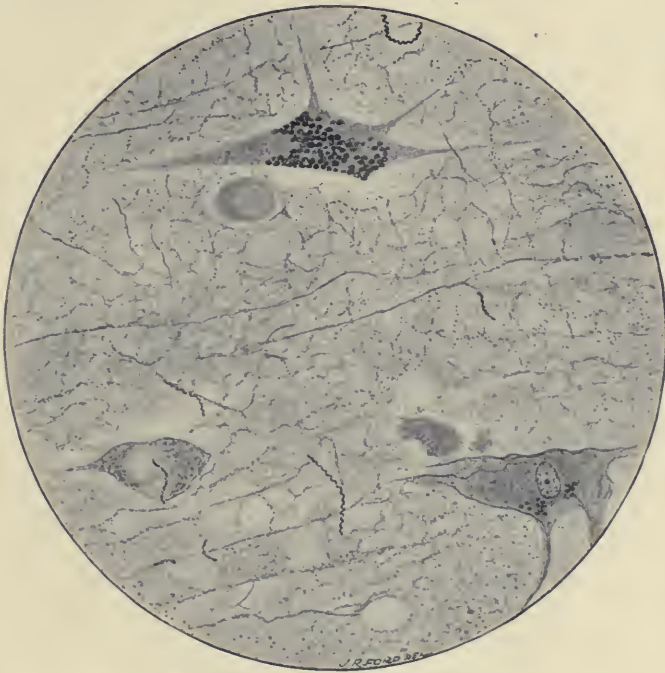


FIG. 1.—Section from frontal region of Case 2 (M. A. H.). Zeiss $\frac{1}{12}$ and No. 6 compensating eyepiece. Noguchi's stain.

Spirochætes.

- | | |
|-----------------|--|
| Dark ground ... | Numerous <i>Spirochætæ pallidæ</i> in the frontal and central regions. |
| Sections... .. | Large foci in frontal area, small in the central; spirochætæ mainly superficial. |

(*Vide* fig. 1.)

Case 3.—R. M., male, aged 35. Duration of mental symptoms indefinite; stopped work (coal miner) three days before admission; admitted August 3

1912, died January 13, 1914. Patient was quite demented, and had no knowledge of his surroundings.

Autopsy.—Brain weighed 1,140 gm. Considerable excess of subdural fluid. Pia-arachnoid thickened and opaque, granulations in the fourth ventricle, grey matter very atrophic.

Microscopic appearances.—Meninges here and there show a very slight cellular infiltration. In the brain no distinct perivascular accumulation of cells, though in places there appears to be a slight increase of these cells. The pyramidal cells show much atrophy and degeneration; slight increase of glial cells.

Spirochaetes.

Dark ground ... One or two degenerate objects seen, but it was doubtful whether they were spirochaetes or not.

Sections ... None found.



FIG. 2.—Section from frontal region of Case 4 (S. C.).

Case 4.—S. C., female, aged 40. Duration of symptoms, two months; admitted September 24, 1913, died January 13, 1914. Patient had no interest in her surroundings and was quite demented. She gave birth to a child on October 20, 1913, which, however, only lived a day. It had a diffuse cirrhosis of the liver with small-celled infiltration.

Autopsy.—Brain weighed 1,180 gm. Pia-arachnoid thickened and opaque, large arteries atheromatous, grey matter thin and congested, granulations in the fourth ventricle and lateral ventricles.

Microscopic appearances.—Meninges thickened and œdematous, slight infiltration with lymphocytes and plasma-cells, extravasation of red cells, proliferation of the endothelium of the vessels. In the cerebral substance the perivascular infiltration is very slight, the pyramidal cells show some degeneration but are normal in number.

Spirochætes.

Dark ground ... Spirochætes very numerous (two or three in each field) in the frontal and central regions.

Sections ... In places spirochætés very numerous.

(Vide fig. 2.)

Case 5.—J. T., male, aged 47. No previous history obtainable, admitted April 23, 1913, died January 17, 1914. Grandiose delusions; just before death had several convulsive seizures.

Autopsy.—Brain weighed 1,470 grm. Pia greatly thickened, opaque, and congested. Vessels showed patches of atheroma. On section grey matter yellowish and atrophic. Coarse granulations in fourth ventricle.

Microscopic appearances.—Meninges showed a moderate infiltration mostly of mononuclear cells, with a few plasma-cells. In the brain, general perivascular infiltration which included large numbers of plasma-cells.

Spirochætes.

Dark ground ... Spirochætes few in number and rather degenerate.

Sections ... None found.

Case 6.—J. T. B., male, aged 34. Duration of mental symptoms three weeks, admitted December 29, 1913, died January 6, 1914. History of syphilis. The clinical diagnosis was "cerebral syphilis," ptosis of left eyelid, left pupil dilated. Patient confused, violent, and resisted any attempt to examine him.

Autopsy.—Brain weighed 1,405 grm. Dura thickened and subdural fluid increased. Pia very vascular and adherent, grey matter congested, granulations along floor of fourth ventricle.

Microscopic appearances.—Marked cellular infiltration of the pia-arachnoid. The blood-vessels were engorged but their walls normal. Perivascular infiltration in the cortex was marked in places; plasma-cells were few in number. No obvious proliferation of neuroglia. Pyramidal cells were considerably shrunken.

Spirochætes.

Dark ground ... Spirochætes found in the frontal and central areas.

Sections ... None found.

Case 7.—A. R., female, aged 46. Duration of mental symptoms three months; admitted October 6, 1913, died January 8, 1914. Happy and fatuous; clinical diagnosis "dementia paralytica." Wassermann reaction positive in blood and cerebrospinal fluid.

Autopsy.—Brain weighed 1,140 grm. Enormous increase in subdural fluid, membranes slightly thickened, grey matter pale and atrophic, granulations in the fourth ventricle very marked.

Microscopic appearances.—Slight cellular infiltration of the pia-arachnoid. Vessels in the cortex showed only a moderate infiltration of their sheaths; though in one or two places it was more pronounced. Infiltration consisted of large mononuclears with a few plasma-cells. Pyramidal cells were decreased while glial cells were proliferated.

Spirochætes.

- (Dark ground ... Numerous spirochætes in the frontal and central and visual areas; most in the frontal regions.
 Sections ... Several foci with numerous spirochætes in frontal area.
 (Vide figs. 3 and 4.)

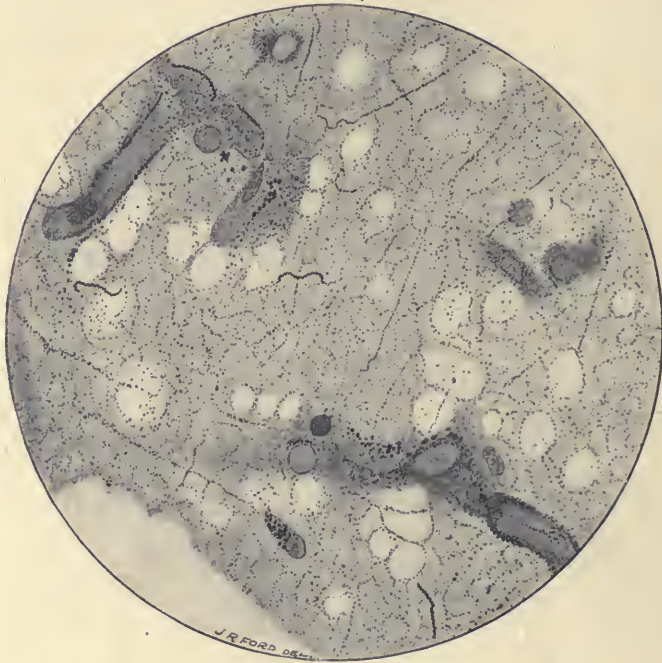


FIG. 3.—Section from frontal lobe of Case 7 (A. R.).

SUMMARY.

It will be seen that seven cases of "dementia paralytica" were examined, and that in six of these spirochætes were found by the dark-ground method, although when sections of these positive cases were cut the organisms were only detected in three. It is thus obvious that the latter method presents much greater difficulties than the former, the spirochætes being found only when they are numerous. Five cases also were examined in which the symptoms suggested a diagnosis of "dementia paralytica." This diagnosis was, however, found on section to be incorrect. No spirochætes were found.

These results do not illustrate the distribution of the spirochætes

over the whole cortex, because specimens were sent from a few regions only. It was, however, usual to find the organisms in all specimens sent when success was obtained with one.

All the cases examined had exhibited relatively acute manifestations before death, and the brains with one exception were not markedly wasted. The lesions on the whole appeared to be recent.

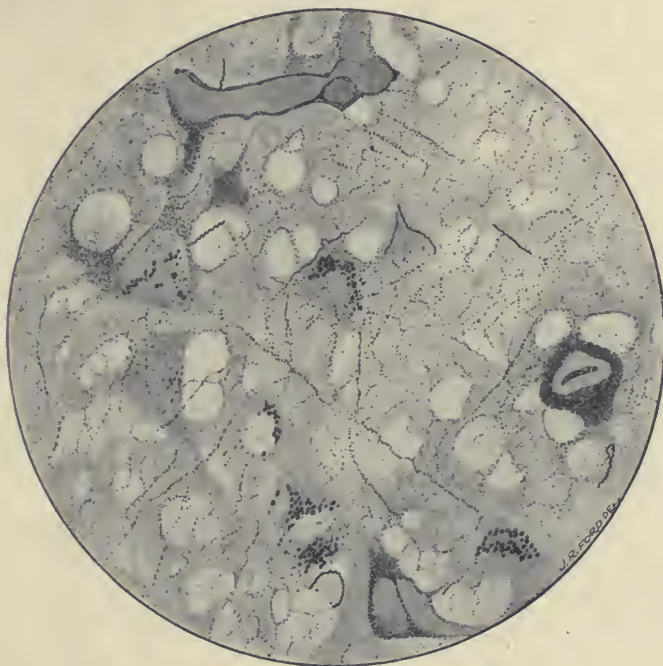


FIG. 4.—Section from frontal lobe of Case 7 (A. R.).

As already mentioned¹ the spirochætes were always confined to the grey matter; in one case only was a single specimen seen in the meninges. They were more or less superficial, and no constant relation could be observed between them and nerve-cells or blood-vessels. Some spirochætes indeed appeared to be applied to nerve-cells, but this distribution was not striking. Further no connexion was apparent between the organisms and cellular infiltrations; indeed they appeared to be scattered quite fortuitously about the superficial layers of the cortex.

It may be remarked that the drawings by Mr. J. R. Ford give an extremely accurate impression of the appearance of the sections under the microscope.

¹ McIntosh, J., and Fildes, P. *Brain*, 1914.

SOME CASES OF A "CROSSED REFLEX" ASSOCIATED WITH PAIN: THE BEARING OF THE CROSSED REFLEX UPON THE THEORY OF THE EXISTENCE OF AUTOMATIC SPINAL CENTRES.

BY E. D. MACNAMARA AND E. B. GUNSON.

THE five cases, the notes of which are subjoined, are, in the main, presented for record for two reasons; firstly, that they afford examples of a reflex of rare occurrence, and secondly, because the phenomenon of pain which occurred on the application of the stimulus eliciting the reflex in four of the cases has not, so far as we are aware, been previously described. The cases are also presented as data for the further elucidation of the problem as to whether such movements as are described may be regarded as evidence for the existence of automatic spinal centres.

Case 1.—The patient, a male, aged 15, was admitted to the West End Hospital for Nervous Diseases on May 16, 1912. Two months before admission he had suffered from loss of speech, loss of memory and mental dulness. These symptoms had lasted for fourteen days and the patient then completely recovered. He remained well for four weeks, when the symptoms recurred. On admission the history was that the patient had not spoken for a week, and that he had vomited once before breakfast. He took very little notice of his surroundings, and his face was expressionless. He appeared to understand what was said to him, and carried out simple instructions. He gave his name and address correctly, but showed no further inclination to speak. On examination there was no evidence of loss of power or of sensation. There were no abnormal movements, and co-ordination was good. There was well marked optic neuritis in the right eye. The superficial reflexes were very active, and equal on the two sides. The supinator, knee- and ankle-jerks were brisk, and equal on the two sides. There was a tendency to ankle-clonus on the right side. Oppenheim's and Gordon's signs were present on the left side only. Incontinence of urine had occurred on two occasions.

The boy gradually became more dull, and entirely refused to speak. The optic neuritis became more marked on the right side, and also gradually began on the left. It was thought possible that there was a cerebral tumour affecting the right frontal region. On June 6 Mr. Ballance performed

craniectomy over this region. There was no obvious increase of intracranial pressure. The dura was opened, but no tumour was found. After the operation the patient became very suspicious, resented all efforts made on his behalf, and frequently refused food.

It was now first noticed that on grasping firmly the quadriceps extensor muscle with the thumb and fingers immediate flexion at the opposite hip-joint took place. The reflex was equally present on each side. No response was produced by merely stroking the thigh or by percussion of the muscles or bones. There was no movement at the hip-joint of the side grasped, though dorsiflexion of the great toe on this side did occur. It was a particularly remarkable fact that elicitation of the reflex apparently caused considerable pain, and was much resented by the patient.

The patient was discharged from hospital about one month later. By that time his symptoms had all cleared up, and the crossed reflex had disappeared. The swelling of the discs had very largely subsided. He remained well until December, 1913, and presented no symptoms or abnormal physical signs, save that the discs suggested a past papillo-œdema. At the beginning of December, 1913, he began to be silly and to do stupid things. He was forthwith admitted to the hospital, and soon showed the symptoms of negativism which had been so marked before. The cross reflex reappeared, but the movement was of smaller excursion and was unattended by pain. There were no other abnormal physical signs, and the papillæ were not more swollen. The symptoms gradually abated, and the patient was quite well by the middle of January, 1914. At no time during his illness had anything abnormal been discoverable in any of his other organs.

Case 2.—The patient, a male, aged 29, was admitted to the West End Hospital for Nervous Diseases on September 2, 1912. This patient had, according to his history, never been intellectually very bright. He had contracted syphilis four years previously. In May, 1908, he had an attack of generalized convulsions. He was semiconscious for about two weeks, and during that time had a series of epileptiform attacks. He was then put on bromide, and remained free from fits for some ten months. The fits then recurred, and he has had them occasionally ever since. In 1910 an operation was advised, but was refused. X-rays at that time showed thickening in both frontal regions, but no tumour mass. In February, 1912, a positive Wassermann was obtained, and patient was dosed with salvarsan, and again in May and June. He also had inunctions of mercury. During the last four years he had had frequent and severe frontal and occipital headaches and occasionally had vomited, without other dyspeptic symptoms.

On admission to the hospital the patient was dull and lethargic, with occasional choleric outbursts. His memory was poor, and he was conscious that it was failing. He could not detect strong smells through either nostril. A double papillo-œdema was present, and the discs also suggested an early stage of atrophy. He could perceive acids on both sides of his tongue, but could not taste sugar or salt. So far as the rest of the body was concerned there appeared, on the sensory side, to be no loss of any faculty for the

perception of any sort of stimulus. Stereognosis was also good. On the motor side there were no marked abnormal physical signs. There was no weakness, wasting, spasticity or flaccidity, but there was some inco-ordination affecting the upper extremities. The knee- and ankle-jerks were exaggerated equally on both sides. There was no ankle-clonus. The abdominal reflexes were absent on both sides. The plantar reflexes were flexor. On grasping the quadriceps extensor mass on one side slight but definite flexion occurred at the opposite hip, and was most evident on the right side. A remarkable feature was that the patient complained of the pain caused by grasping the quadriceps. There was occasionally incontinence of urine. At this time the Wassermann reaction was negative. In the cerebrospinal fluid 1'3 lymphocytes were counted per cubic millimetre. A fit occurred at this time, and it was noticed that the left arm first became rigid in extension, and that the head and eyes turned to the left before the convulsion became generalized. On November 26 the patient died, and on *post-mortem* examination a subcortical cystic glio-sarcoma was found in the upper part of the right frontal lobe extending back almost to the Rolandic area.

Case 3.—The patient, a male, aged 15, was admitted to the General Infirmary, Leeds, on May 10, 1913. In May, 1912, the patient began to suffer from severe frontal headache, with vomiting, shortly after food. General malaise and constipation were associated with these symptoms. They persisted for a week, and then completely disappeared. A similar attack occurred seven weeks later, and lasted two weeks. A third attack occurred four weeks after the second, and followed the same course for a week, when the patient was seized with a severe cramp affecting the right foot, spreading slowly upwards until the whole of the right side was involved. The cramp was accompanied by weakness, and after lasting for an hour passed off in inverse order. There was no loss of consciousness. The following day the other symptoms subsided. A fourth and fifth attack occurred, at intervals of a month, like the third, and associated with cramp and weakness of the right side, each attack lasting about one week. A sixth attack occurred in February, 1913. With the onset of the cramp the patient became dazed, and was led to bed. He became semi-conscious, his eyes became fixed, and he screamed out frequently. On the following day the symptoms had subsided. The last attack, five weeks before admission, was very slight, and was accompanied with cramp and some transient weakness of the left leg. In the intervals between the attacks the patient had followed his employment and enjoyed good health.

On admission the patient presented no symptom of mental disturbance. Double optic neuritis was present, and was more marked on the right side. On the sensory and motor sides he presented no abnormalities. The supinator, knee- and ankle-jerks were present, and were equal. The superficial reflexes were present and were active, and equal on the two sides. The flexor response was present on the two sides. On grasping the left quadriceps extensor mass slight flexion occurred at the right hip and slow extension of the great toe on the right side. There was no movement of the other toes or at the left hip.

On grasping the right quadriceps there was no response on either side. The provocation of the reflex on the left side caused considerable local pain; stimulation of the right side was quite free from pain. There was no symptom connected with the sphincters. Examination of the other systems revealed nothing abnormal. The patient remained in the hospital for seven weeks, during which time the optic neuritis completely subsided, and there was no return of symptoms.

Case 4.—The patient, a female, aged 10, was admitted to the General Infirmary, Leeds, on June 12, 1913. The patient had not been well for six months. Two weeks before admission there had been headache, giddiness and occasional vomiting. Ten days before admission an attack of convulsions occurred affecting the face and the upper and lower extremities. Since that time the patient had remained dazed, and had not spoken or taken notice of her surroundings.

On admission the patient was drowsy, but when roused understood what was said to her and performed simple movements. She did not speak. On examination an external strabismus was found on the right side and an internal on the left. Double optic neuritis was also present. There was paresis of the lower part of the right side of the face. There was very little voluntary movement of the limbs, which were rather flaccid. The abdominal muscles were also relaxed. There was, however, some degree of rigidity about the neck. The supinator jerks were present. The knee- and ankle-jerks were absent. Kernig's sign was present on both sides. The abdominal reflexes on the right side were active, but on the left were very feeble. Oppenheim's, Gordon's and Chaddock's signs were absent on both sides, except that Oppenheim's was occasionally present on the right side. On grasping the right quadriceps extensor mass there sometimes occurred slight flexion at the left hip, while there always occurred dorsiflexion of the right big toe and frequently also dorsiflexion of the left big toe. On grasping the left quadriceps mass no movement was produced at either hip, but there was always dorsiflexion of the right big toe, and sometimes dorsiflexion of the left big toe. Elicitation of the movement on either side caused great pain. The patient died on June 30, and on *post-mortem* examination extensive tubercular meningitis was found. The cerebellum was also found to be the seat of a few minute scattered tubercles.

Case 5.—The patient, a female, aged 8, was admitted to the West End Hospital for Nervous Diseases on March 6, 1913, for paralysis of both legs dating from birth. The patient had been a full-time child, and her birth had been normal. She had never been very intelligent, and has never talked properly. She had never walked or even stood up, and assisted progression was of the cross-legged type. The sphincters have always been well under control.

On examination there was found to be some degree of spasticity of both legs and of the right arm. Microkinetic movements of all the limbs were present. The tendon-jerks were all exaggerated, and both plantar reflexes

were of the extensor type. A Foerster's operation was performed by Mr. Laming Evans on June 24, and the spasticity of the limbs became slightly less. In this case tickling the sole of the left foot produced a movement of flexion of the right thigh, while tickling the sole of the right foot produced no movement. Grasping the muscles of the calf or the front of the thigh of either leg produced flexion of the right thigh but not of the left. In this case there was no associated pain.

To emphasize certain salient points in the histories of these cases we have tabulated them.

No. of case	Place at which stimulus was applied and character of stimulus	Resulting movement	Whether pain was present or not	Whether extensor response as elicited by ordinary methods was present	How case terminated	Character of lesions
1	Grasping the quadriceps extensor mass on either side	Flexion at opposite hip and dorsiflexion of great toe on the side stimulated	Pain was present	No	Symptoms cleared up	? lesion of right frontal region.
	Stroking the skin	No movement				
2	Grasping the quadriceps mass on either side	Flexion at opposite hip. No movement of the big toes	Pain	No	Death	Tumour right frontal region.
3	Grasping quadriceps mass on left side only	Flexion of opposite hip and dorsiflexion of opposite big toe	Pain	No	Symptoms cleared up	?
4	Grasping quadriceps mass on right side	Flexion of opposite hip and dorsiflexion of right big toe and occasionally of left big toe	Pain	Extensor response elicited by ordinary methods	Death	Extensive tubercular meningitis.
	Grasping quadriceps mass on left side	No movement at hips, but dorsiflexion of right great toe and occasionally of left				
5	Grasping the quadriceps mass or the calf on either side	Flexion at right hip. There was no movement at the left hip	No pain	Extensor response elicited by ordinary methods	Symptoms remained much as they had always been	Double cerebral sclerosis.
	Tickling the sole of the left foot	Flexion at right hip				
	Tickling the sole of the right foot	No movement at either hip				

An analogous reflex has been described by Levi-Bianchini [3]. According to him, in certain cases of mania, if the muscles of the calf

be squeezed on either side of the tibia, as the patient lies in bed, there results an immediate and energetic contraction of the quadriceps femoris. He writes that in most cases the reflex may be obtained on both sides; in others, however, it can only be obtained on one side. Gordon [1] had previously described an extension of the big toe occurring in patients with damaged pyramidal tracts on pressure being applied to the muscular mass constituting the calf. Guillain [2] has reported the presence of a contralateral flexion of the thigh upon the abdomen, and of the leg upon the thigh with abduction of the limb upon compression of the quadriceps femoris in meningitis of varying etiology. Marie and Foix [4] described movements, in certain cases, additional to those observed by Gordon, in which, by pressure upon the calf the great toe extended, the foot dorsiflexed upon the leg, the leg flexed upon the thigh, and the thigh upon the abdomen. Occasionally, also extension of the other leg was noticed. In cases of compression paraplegia, of disseminated sclerosis and of syringomyelia, the same observers have observed that on forcible flexion of the toes the same movements of shortening of the leg are produced, and may be followed by extension of the other leg. This movement appears to be analogous to the "stepping reflex" described by Sherrington [10] and Philipson [8] as occurring in animals, and which has otherwise been called the "crossed extension reflex." Marie and Foix conclude that such complex movements in fact represent the automatic movements of walking, that the elementary movements of walking can, by excitation here and there of the leg, be resolved into isolated muscular contractions, and that this automatism exists normally but becomes exaggerated by certain pyramidal lesions. They are further of opinion that Babinski's sign belongs to the totality of the complex automatic movements which together constitute the mechanism of progression, since at the moment when in walking the leg is, in part, flexed in the act of raising it from the ground the great toe is dorsiflexed. The sign is described as the minimal reaction to excitation.

These views are not universally accepted. V. Woerkom [11] lays stress on the sort of stimulus applied to arouse the reflex movement. For instance, the passive flexion of one limb, in which there is no association of pain, provokes the extension of the other (as, he says, is proved by the experiments of Freusberg and Sherrington), whereas a painful stimulus does not produce contralateral movements (and in fact it inhibits them), but rather a simple movement of withdrawal from the stimulating agent. He points out, however, that the contracting

muscles are the same for the movement of withdrawal as for that phase of walking which consists in the removal of the foot from the ground. To explain the mechanism of the extensor response v. Woerkom argues from certain ontological predicates. The big toe early in its development is adapted to perform prehensile functions. The position for prehension is scarcely compatible with comfortable or efficient progression. To overcome this incompatibility the extensor longus hallucis comes into action, for it has abductor as well as extensor functions. This function is not shared with the extensors of the other toes, and later on in life, when the art of walking has been acquired, is lost. In the process of adaptation to walking, which is presumed to have occurred when our ancestors exchanged arboreal life for one passed on the ground, the muscle has acquired an extensor function which is no longer a useful one when progression and not prehension becomes the important work of the toes. For progression the big toe acts with its fellows, for prehension in opposition to them. In babyhood, before progression is necessary, the big toe acts, on stimulation of the plantar surface of the foot, in opposition to the other toes; and similarly in organic maladies of the nervous system this ancient function again appears. To quote v. Woerkom's own words the movement is, "The vestige or revival of a lost function which consisted in the adaptation of the individual's foot to progression on the flat, and in which the great toe was still capable of taking a position of opposition to the other toes." Marinesco and Noica [5] reach the conclusion that normal subjects do not react, in respect of painful excitations, as do those suffering from spastic paraplegia who have almost completely lost the power of voluntary movement, whether they have or have not preserved sensibility to pain. In the normal individual movement is always in the direction of removing the limb from the disagreeable or painful excitation. This is not so of the movements which occur in spastically paraplegic individuals, which have not a character suggestive of flight from danger. The movements need not be accompanied by sensation, and can therefore be provoked unknown to the patient. Further the range of the movements diminishes if the limb be rendered anæmic by an Esmarch's bandage, and is exaggerated when blood is readmitted into the limb. On the other hand, true movements of defence are exaggerated when the limb is rendered anæmic, and are associated with much pain. Rossenda [9] relates a case of tabes in which all the tendon and bone reflexes were absent, as were also the cutaneous reflexes, including the plantar as ordinarily provoked or evoked. If, however, the

sole of the foot were forcibly stroked with the handle of a percussor, or if the toes were overflexed, certain movements occurred. The stroking of the sole and the flexion of the toes were not felt as such, though associated both with the stroking and the flexion there was much pain, which the patient compared to the lightning pains he occasionally experienced at other times. The movements consisted in energetic flexion of the thigh upon the trunk, of the leg upon the thigh, and of the foot upon the leg. While these movements of flexion went on extension of the opposite limb occurred, provided it had beforehand been placed in an attitude of flexion upon the abdomen. Rossenda is of opinion that, conformably to the views of Marie and Foix, the retraction which in certain pathological conditions occurs in consequence of excitation of the sole of the foot or of the joints of the toes, and which may or may not be associated with extension of the other leg, should be considered as due to cord automatism and not as a simple reflex. In a further communication Marinesco and Noica [6] arrive at the conclusion that the phenomena which occur on the side excited, or by propagation on the opposite side, vary with the intensity of the excitation and secondarily with the position of the limbs before excitation. In other words, these authors conclude that there does not exist in the cord a co-ordinating motor centre having some degree of independence in the choice of movements, or that if such a centre exists it is absolutely subordinate to the intensity of the excitation, and to the position of the limbs at the moment of excitation. Pastine [7] does not think that the extensor response can be placed among the automatic movements of walking, and that it occurs equally with movements, voluntary or reflex, of extension of the lower limb.

It will be noticed that in every one of our cases grasping the muscular mass on the front of one thigh resulted in a movement of flexion at the opposite hip-joint; that is a "crossed reflex" was present. This movement of flexion at the hip was, in Case 1, associated with dorsiflexion of the great toe of the opposite side to that upon which flexion at the hip occurred, that is the dorsiflexion of the toe took place on the side to which the stimulus was applied. In Case 3 the dorsiflexion of the great toe and the flexion at the hip-joint took place on the same side, that is on the side opposite to the one stimulated. In Case 4 dorsiflexion of the great toe on the side opposite to the one stimulated always took place, and dorsiflexion of the great toe on the side stimulated occasionally took place, a condition of affairs combining the characteristics of Cases 1 and 3. In Cases 2 and 5

no movement of the toes was noted. It appears to us difficult to regard a crossed reflex as a merely defensive one, presuming always that neither limb is by any sort of palsy deprived of the power of movement. It is, of course, the case that a movement of withdrawal of a limb occurs when any part of it is unpleasantly stimulated, unless such movement is inhibited from higher centres. It may be argued that such movements of withdrawal persist as habits and may at length involuntarily occur as reflex movements when the limb is stimulated not unpleasantly. It cannot, however, be so readily assumed that a movement of the limb opposite to the one stimulated associated with no movement of the stimulated limb is a movement of mere withdrawal or of defence. Indeed, supposing the motility of the stimulated limb to be unaffected, it is hard to offer any explanation other than that such a movement is one of the series of movements involved in progression and may, therefore, be taken for what it is worth, as supporting the hypothesis of the existence of automatic spinal centres. Considering in addition to the crossed movement of flexion at the hip the associated movement of the big toe, occurring in Cases 1, 3 and 4 of our series, we find ourselves in a difficulty in dealing with this problem, since in Case 1 the movement of the big toe was not on the side of the flexion of the hip, in Case 3 it was on the side of the flexion of the hip, and in Case 4 it was sometimes on the side of flexion and sometimes on the opposite side. From such a jumble of occurrences in so small a number of cases it is hard to draw any inferences, but we doubt if any that might be drawn could be made to support the hypothesis of the existence of spinal centres. It is true that the movement of toe and thigh in Case 3 might be harmonized and regarded as simultaneous movements of progression, since while the thigh is flexed upon the trunk as it is being brought forward in progression the great toe tends towards extension, in order, as we think may fairly be presumed, to better clear the ground. But such an explanation will not fit Case 1, for while a thigh is moving forward in progression the great toe of the opposite foot tends towards a movement of flexion, applying itself to the ground preparatory to the shove off of the foot from the ground. If the movement in Case 3 was normal to an automatic act of walking the movement in Case 1 was not. In Case 4 movements of the toes occurred indifferently, and cannot be cited in favour of automatism. It will be noted, however, that in Cases 1, 2 and 3 the extensor response could not be elicited by the ordinary methods employed; it did not occur as part of a movement of withdrawal from stimulation; and this fact, coupled with the occurrence of the movement simultaneously, with flexion of a thigh,

suggests to us that the movement might be regarded rather as part of automatic progression than as one of defence. In short, facts from these cases may be adduced in support of either hypothesis. Marie and Foix (*vide supra*) regard an extensor response as a minimal reaction, the complete reaction containing in addition to the movement of the toe flexion of the thigh. We would point out that, if this be so, we obtained in Cases 2 and 5 a reaction in which the minimum did not occur, but in which another feature of the reaction did occur. We think that the inference must be that it is incorrect to speak of the extensor response as a "minimal reaction," since we should in that case have a state of affairs in which the greater did not contain the less. We believe, accepting for the moment the existence of the automatic spinal centres, that we are only justified in regarding one movement as co-ordinate with the other; the extensor response occurring commonly and the complete crossed reflex but rarely.

We desire particularly to draw attention to the very remarkable association of pain with the occurrence of the reflex in Cases 1, 2, 3 and 4. The amount of pain appeared wholly disproportionate to the character of the stimulus applied. In a normal individual such a stimulus produces no pain whatsoever and in several hundred patients suffering from a variety of maladies we have failed in applying a like stimulus to elicit pain. The pain was located at the site of the place where the muscular mass on the front of the thigh was grasped. In Case 1 the site of the lesion was supposed to be the right frontal region. In Case 2 the site of the lesion was the right frontal region. In Case 3 no particular locality could be assigned to the lesion. In Case 4 the lesion was a diffuse one and in Case 5 there was a presumption in favour of extensive cerebral sclerosis.

We are indebted to Drs. Wardrop Griffith and Maxwell Telling for permission to record Cases 3 and 4 respectively.

REFERENCES.

- [1] GORDON. *Rev. neurol.*, 1904, tome xii, p. 1083.
- [2] GUILLAIN. *Bull. et Mém. de la Soc. méd. des Hôp. de Paris*, 1912, tome xxxiii, p. 711.
- [3] LEVI-BIANCHINI. *Rev. neurol.*, 1912, tome xxiii, p. 393.
- [4] MARIE et FOIX. *Rev. neurol.*, 1912, tome xxiii, p. 660.
- [5] MARINESCO et NOICA. *Rev. neurol.*, 1913, tome xxv, p. 516.
- [6] *Idem. Ibid.*, 1913, tome xxvi, p. 134.
- [7] PASTINE. *Rev. neurol.*, 1913, tome xxvi, p. 403.
- [8] PHILIPSON. "Travaux du Laboratoire de Physiologie de l'Institut Solvay, Brussels," 1905.
- [9] ROSSENDA. *La Riforma Medica*, 1913, vol. xxix, p. 561.
- [10] SHERRINGTON. *Proc. Roy. Soc. Lond.*, 1905, vol. lxxvi, pp. 160, 269; *ibid.*, 1906, vol. lxxvii, p. 478; *ibid.*, 1907, vol. lxxx, p. 53, *et seq.*
- [11] VAN WOERKOM. *Rev. neurol.*, 1912, tome xxiv, p. 285.

A CASE OF MOTOR DYSPRAXIA AND PARAPHASIA: AUTOPSY: TUMOUR IN SUPRAMARGINAL CONVOLUTION.

BY E. G. FEARNSIDES, M.D., M.R.C.P.

Beit Memorial Research Fellow ; Assistant Physician to the Hospital for Epilepsy and Paralysis, Maida Vale ; late Medical Registrar to the London Hospital.

ALTHOUGH the manifestations which are included under the term motor dyspraxia are found not infrequently in cases of hemiplegia, aphasia and other cerebral disorders, the number of cases which have been fully investigated both clinically and pathologically is still small. Moreover, in the majority of cases which have been reported in the literature motor dyspraxia has been one only of a series of manifestations, and at necropsy multiple lesions have usually been found. In the patient who forms the subject of this note the clinical interferences were limited to motor dyspraxia, dysgraphia, paraphasia, and amnesic aphasia, and at autopsy a small, well localized, secondary carcinomatous nodule in the left supramarginal convolution surrounded by recent cerebral softening was found. The case, although incomplete from a pathological point of view owing to the fact that a detailed microscopic investigation of the fibres destroyed by the tumour was impossible, seems to be one of considerable importance for the localization of these interferences in the cerebral hemispheres.

Wilson [6] defines *motor dyspraxia* as "the difficulty in performing certain subjectively purposive movements, or movement complexes, with conservation of motility, of sensation, and of co-ordination." Liepmann [3] terms the difficulty in finding words *amnesic aphasia*, and gives the name *paraphasia* to the difficulty with speech characterized by "omissions, duplications, perseveration to earlier syllables, anticipation of later syllables, sliding off into words related in sound and sense, fusion of parts of suitable words with those of similar sound and similar sense, and loss of sequence in words owing to the action of accidental sensory impressions."

Whilst under observation from a clinical point of view the patient was for twenty-one days a satisfactory subject, and during this time

his condition altered little: Twenty-four days before death, however, weakness of the left half of the body and hebetude appeared, probably owing to the development of cerebral softening around the tumour.

At the International Congress of Medicine in London in 1913, Liepmann [3] said, "the region which is by far the most frequently affected in well developed apraxia is the left parietal region. This I have proved by a study of twenty-six cases of my own and of the whole of the literature on apraxia. Indeed there are sufficient cases of apraxia in which only lesions of the parietal lobes have been found." Kleist [1] in 1911 analysed the findings at necropsy in twelve recorded cases of ideo-kinetic dyspraxia, such as this patient exhibited, and found that in all lesions of the supramarginal convolution had been present; in eight of these other lesions also existed. In a case reported by Strohmayer [5] in 1903 severe motor dyspraxia affecting all four extremities, paraphasia, loss of initiative, and considerable difficulty with reading and writing were associated, and at autopsy a cyst 5 cm. in diameter was found in the left supramarginal convolution. Isolated lesions of vascular origin were also found in this region in two cases reported by Kroll [2] in 1910 and in one reported by von Stauffenberg [4] in 1911. These four cases all showed clinically severe motor dyspraxia of all the extremities and both halves of the trunk, difficulty with reading, inability to copy, difficulty in writing to dictation, paraphasia, and considerable loss of memory; and at autopsy cyst formation or cerebral softening consequent on interferences with the blood supply of the supramarginal region on the left side was found in each. Von Stauffenberg [4] sums up his conclusions "lesions of the lower portions of the parietal lobe which do not involve either the angular gyrus or first temporal convolution, but affect the subcortex almost down to the lateral ventricle, regularly give rise to apraxia and an interference with the mechanism of speech, characterized by paraphasia and gross interferences with reading and writing but do not affect the understanding of speech." The findings at autopsy in my case confirm his statement that "disease localized to the supramarginal convolution on the left side can cause apraxia." Nowhere in the literature, however, have I been able to find any record of a case where a well localized neoplasm, either primary or secondary, has given rise to motor dyspraxia and paraphasia.

In this case it is also noteworthy that, although from the appearance of slight proptosis, paralysis of the external rectus and paresis of the internal rectus muscles, and the distortion of the outlines of the sella turcica as seen in the radiogram, the presence of secondary carcinoma

in the region of the pituitary gland was diagnosed during life and its presence confirmed at *post-mortem* examination, no signs of super-pituitarism or subpituitarism were present; yet, as seen in the microscopical specimens, practically the whole of the three lobes of the pituitary gland were infiltrated by growth and little normal glandular tissue could be discovered.

Sidney T., married, engineer's fitter, aged 41, was admitted to the London Hospital under the care of Dr. Lewis Smith, on August 17, 1914, and died on September 29.

Between 1903, when he married, and 1913 his health was uniformly good. About February, 1914, he began to complain to his wife that his habitual skill with his tools was failing; he became depressed and irritable, but his health remained fair until June, 1914. During the last week of that month his left wrist swelled, and the skin over it became red, shiny, and tender. He saw his local doctor, who diagnosed gout and kept him from work for seven days. Three days after his return to work he developed a left-sided headache. The headache was severe, persistent, and kept him awake at night time; in bed he was restless and tossed about. On July 10 he began to "see double"; he then attended at an Eye Hospital, where he was found to have paralysis of the left sixth cranial nerve and a certain amount of proptosis on that side. During the month of July, speech was not affected, memory was good, and yet he "thought he was going out of his senses," and became more irritable and more depressed. About 10.30 p.m. on August 3, he had a seizure; "for a minute or so he went stiff, his eyes rolled, he became black in the face and foamed at the mouth." After the seizure he complained that his headache had increased, he tossed about but only partially roused. Half an hour later, about 11 p.m., he had a second similar attack lasting a minute or so. He then remained unconscious until 12.45 a.m. on the 4th, when he suffered from a third similar, but more severe, attack in which he passed water. For the next eight hours he lay drowsy or asleep, and did not know where he was. On August 4 the pains in his head were extremely severe, diplopia had become more troublesome and speech had altered. He was kept in bed from the 4th until the 9th, and gradually, despite the pains in his head, "seemed to become his old self again."

During the week, August 10 to 17, he gradually "went downhill." His memory failed and "he would wander and lose his words, although his mind was otherwise clear." His wife said that he seemed to be unable to recognize that he was only addressing her as soon as he began to talk about other people's affairs; "when talking at home to me alone, he would speak of my wife Annie just as if he were in company." On the 10th, for instance, he was talking to his wife about the affairs of his brother-in-law, when he suddenly remarked "now my wife Annie cannot help me"; on the same day he was found gazing into a cupboard, and when his wife asked him what he was doing he remarked "I don't know why I look in there, I must be mad."

On the 16th he lay in bed all day complaining of intense pain in the left side of his head.

He denied all venereal infection, and the Wassermann reaction both in the serum and cerebrospinal fluid was negative. At the age of 17 he had suffered from diphtheria. His wife, who was alive and well, had had two children, born in 1904 and 1907, who survived and were healthy.

The patient was a well developed, pale, thinly covered, right-handed man of 41, showing signs of recent wasting. On admission the temperature tended to be slightly irregular and varied from 97° to 99° F. The apex beat of the heart was felt in the fifth space just inside the midclavicular line. The area of cardiac dulness was not increased, there was no cardiac displacement, and the heart sounds were clear. The wall of the radial artery was just palpable, but the tension was not raised. The rate of the pulse varied from 60 to 80 beats per minute. The liver and spleen could not be felt and to percussion were not enlarged. The quantity of urine passed in twenty-four hours varied from 28 oz. to 56 oz.; albumin and sugar were never present. The lymphatic glands above the clavicles and in the axillæ and groins were not enlarged. The fingers were slightly clubbed.

For some days before his admission he had complained of a dry, hacking cough, but had not expectorated. The chest was symmetrically developed, but moved badly in its upper half on the left side. The movements of the lower portions of the chest on the two sides were equal. Tactile vocal fremitus and vocal resonance were unaffected. In front, the percussion note was impaired in the second, third and fourth interspaces on the left side, but was almost normal in the supraclavicular fossa; behind, the note was flat over the upper part of the infraspinous fossa and between the second and fifth thoracic spines and the vertebral border of the scapula, and was impaired over the whole of the upper lobe on the left side. The breath sounds over this lobe were weaker than over the corresponding areas on the right side, and from time to time fine or medium crepitations were heard there. A radiological examination of the chest at this time showed an opacity of almost uniform density of the whole of the upper part of the left side, with displacement of the trachea to the right, but no displacement of the heart. A radiographic plate in addition gave evidence of some consolidation in the region of the root of the lungs. The rate of respiration varied from 20 to 26 per minute.

The knee-jerks were equal and readily obtained. The ankle-jerks were normal, there was no ankle-clonus, and both plantar reflexes gave a flexor response. The wrist- and elbow-jerks were unaffected, and the jaw-jerk was obtained. The abdominal reflexes could be elicited, but were sluggish. The ocular and pharyngeal reflexes were normal. The sphincters were under control, and the movements of the spine were unaffected.

To sensory testing no loss of sensibility was discovered. The light touches of cotton-wool were everywhere appreciated, and could be localized. The pricks of a pin and the tests with hot and cold tubes at varying temperatures elicited accurate replies. The vibrations of a large tuning-fork ($C = 128$) were

well recognized on all four extremities, and the duration of their recognition was nowhere shortened. Recognition of posture and passive movement was unaffected, and without much effort he could identify and give the properties of objects placed in his hands. There was no falling away of the outstretched upper extremities on closure of the eyes.

In the extremities and trunk there was no local muscular wasting, and no change in muscular tone. Movements of normal range and power were possible at all joints, and the patient did not complain of spontaneous twitchings, and showed no other involuntary movements. Gait was little affected, and Romberg's sign was not obtained. The grasps of the hands were powerful and equal.

He complained much of diplopia. Movements of the right eye were well carried out. The left eye was turned inwards. With this eye he experienced considerable difficulty in looking inwards to the right, and was completely unable to look outwards to the left. The left eyeball was more prominent than the right, but there was no ptosis of the upper eyelid, and nystagmus was not present. The pupils were equal, and reacted briskly to light and to accommodation. Facial movements were normal, and the movements of the palate and larynx were unaffected. The trapezii and sternomastoid muscles acted normally, and he suffered from no difficulty in swallowing. The tongue was protruded straight, and could be held steadily.

Smell, taste, and hearing were unaffected. Vision for form, colour, &c., with both eyes was normal, and the visual fields for white and colours were not diminished. On the left side the vessels of the ocular fundus were full and tortuous, and the lamina cribrosa could not be distinguished; on the right the vessels were full, the edges of the disc blurred, and the lamina cribrosa filled. The swelling of the disc, however, measured less than 1 D.

He constantly complained of pains in the frontal region, and said that they were always worse on the left side than on the right. When asked where the pains were situated, he put his left hand over the left orbital and temporal region, and swept it round over the malar bone towards the left ear. He said that the scalp here was tender, and pressure over the left orbit and temple elicited a complaint of "pain." The pains were usually worst in the early morning and after sleep, but were constantly present. He never complained of pain in the occipital region. He said that the pains in his head made him feel sick, but whilst under observation never vomited. On August 3, 1914, he had suffered from three epileptiform attacks; after this date until death he was free from seizures.

He was attentive and, except when the pains in his head were severe, took considerable interest in the happenings of the ward; he was, however, never interested in his fellow patients. He was extremely grateful for the trouble taken in the investigation of his case, and willingly undertook every test. When his headache was severe, he lay drowsy and inattentive, but when addressed would always rouse himself and attempt to answer questions.

Throughout his stay in hospital memory seemed to vary; on some

occasions he could recall events and give details of his illness, work, and past life; on others all efforts of memory seemed impossible. At times he would describe spontaneously the recent events which had happened around him, and on these occasions gave evidence that he could retain recent impressions.

In space and time he was well orientated; he knew the day, hour, and manner of his arrival at hospital, admission, and of the various examinations. In general he was cheerful, but was easily moved to laughter or tears; when the pains in his head were severe, he was irritable, suspicious, and depressed. Except in the matter of words he was not very subject to suggestion. The last phrase of a sentence seemed frequently to be dominant, and he would often repeat several times the last few words made in answer to a question, even though he was not further addressed.

Judgment and the power of reasoning seemed little impaired, despite his difficulty in expressing himself. He associated ideas readily and could appreciate humorous episodes and the point of a story. He was not subject to hallucinations, and never suffered from delusions. He did not complain of worrying dreams or nightmares. He slept well, and, for the greater portion of the twenty-four hours, when left to himself, lay drowsy or asleep.

In eating and dressing himself he was careless, but became annoyed when he dropped food or otherwise dirtied his bed.

He rarely moved from his position in bed, and, except when directly addressed, rarely spoke. Individual words were well pronounced. He could put together spontaneously short reasonable sentences; in each sentence, however, some words were always badly articulated and slurred. Phonation was monotonous. In attempting to give an account of himself such remarks as: "Last Easter, that was in nineteen, let me see, let me see, fourteen, last Easter, last Easter, to the best of my recollection, as far as I can remember, I went to Easter, to Easter, to Lower Edmonton. There lives my wife and my wife's, yes, my wife's, my wife's sister; he is a cabinet maker at Easter, at Easter" . . . were constantly heard.

He signed his name with great satisfaction; the signature, however, was somewhat illegible and tremulous. In writing his address he misspelt words and, after looking at what he had written, rewrote some of the words which he had spelt wrongly or attempted to polish up the letters. To dictation he wrote single words of several syllables correctly, but was unable to take down correctly a sentence containing more than about five words. After writing a complex sentence he would look at the result, and, becoming dissatisfied, frequently crossed out all that he had written, saying "No, that's not right; I can't do it, I'm losing my senses." In writing to dictation perseveration frequently occurred; for example, he wrote "The London hospital hoptal is the the largst largest larst hostal in London."

He enjoyed reading the newspaper to himself, but easily tired. After reading for four or five minutes he would throw the paper aside to take it up again a few minutes later. He seemed to understand what he had read and would attempt in broken phraseology to retail the occurrences of the War, of which he

had just been reading. When asked to read aloud he managed simple words and sentences fairly well, and understood what he had read; long names and unusual words, however, were bungled and incompletely articulated. Frequently too, he mixed up words from different lines of print, making the whole seem an unintelligible muddle.

After considerable hesitation he copied slowly written manuscript with a fair degree of accuracy, but when copying printed matter he made more frequent errors.

He repeated the alphabet without mistake, and could count readily up to a thousand. He knew all the multiplication tables. He found difficulty in calculating. In attempting to deduce his age from the date of his birth he said: "Let me see, I was born in seventy, seventy, seventy-three, yes, that would be eighteen seventy-three when I was born, so that my age, my age, must be. No, I can't do it, I'm sorry, I can't." When asked immediately after this the age of his child born in 1904, he answered without delay "seventy-three," then he paused a moment and said "I have two children, a boy and a girl, I will give you their ages in a minute, let me see, let me see, no I can't do it, no, no," but never found the answer. When asked if one is not 10 years old, he nodded affirmatively and said "Yes, that's right." The question, How old is your wife? was then asked. "My wife will be ten years old in November; no, that's wrong, my wife will be, will be, eleven years old come June" (his wife was born in June, 1874), "oh, dear, oh dear, I think I'm mad."

In answer to the query, How many are nine times eight? he said: "Let me see 3×8 are 24, 4×8 are 32, 5×8 are 40, 6×8 are 48, 7×8 are 56, 8×8 are 64, and 9×8 are 72; yes nine times eight are seventy-two."

On again being asked, How many are nine times eight? he again repeated the eight times table and arrived at the answer seventy-two. On being asked a third time, he recognized that the question was the same, and remarked, "How foolish, how foolish!" and again repeated the table and found the correct answer. For a few minutes then no words were spoken and he was heard to repeat under his breath, the eight times table through, completely twice, as far as nine times eight. He was then asked, How many are eight times nine? To this he answered, "Eight times nine are the same as nine times eight, but I can't remember how many that made."

Without paper he was able to add eight to twenty-seven and readily answered thirty-five, but when asked to add three hundred and twenty-seven and eighteen, he said "That's more difficult, let me see, eight and seven are, no, let me see; oh I can't do it, no, give me the paper," whereupon he wrote "327"

18 and then said "No, it's too hard," and gave up the attempt. He subtracted in his head eight from twenty-seven and gave the answer nineteen, but when given paper and having written down 327 18 could not do the subtraction.

When objects were held in front of him, he preferred to take them in his left hand, but when his attention was directed to his right hand he would take them in this. He could imitate, with either hand or with both, movements made in front of him; but when attempting to carry out a movement with his right hand, the left often moved correspondingly, and frequently he would repeat the movement he had just finished before he attempted to carry out the new movement which he wished to imitate.

To command he could snap his fingers, whistle, make pill-rolling movements, shake his head, nod, laugh, look angry, groan, cough, touch his nose, put out his tongue, show his teeth, take a deep breath, &c. He could also make any movement of expression, beckon, salute, throw a kiss, clasp his hands, make a fist, prepare for fight, &c.

On request he could make simple movements for definite objects without having the object in his hand. He showed well how to knock at a door, count out money, draw a cork, turn a barrel organ, strike a match, with either hand, but in all these actions the movements performed with the left hand were better executed than those with the right; when using the right hand, more joints of the limb and frequently the whole of that half of the body partook.

With more complex orders the results were always less well performed than with simple orders. For instance, when told to put his left hand on his head, the movement was well carried out; but when told to put his left hand on his right ear, he first put his left hand to his left ear, and then put his right hand on his right ear; recognizing, however, that he had not done what he intended, he shook his head, looked around for a moment when a gleam lighted his face and he put his right hand to his right ear and his left hand to his left ear. He was then told to put his left forefinger on his nose, whereupon he put his left hand on his left ear and then placed his right forefinger to the bridge of his nose. At the question, *Is that right?* he put his left forefinger on to his nose, and then quickly put his right hand to his right ear saying, "Now that's it, isn't it?"

On being asked next to make a fist with the left hand, he made a fist with both hands. He was then told to open his left hand, whereupon he opened his left hand, then half closed it, opened his right hand, half closed this, and finally opened both hands.

When asked to make movements as of cutting out with scissors, he made with both hands irregular movements for clumsily using scissors; a moment later, after gazing at his hands, he stopped the movements with his left hand whilst continuing those with the right.

He was able to make any simple movements on request; he touched his ear, scratched the middle of his back, pulled his hair, touched his great toe, tickled himself on command. He was equally certain when asked to touch similar parts of the observer's body. With objects in his hands he could brush his nails, comb his hair, blow his nose, &c. When given a paper knife and asked to show how this should be used, he folded the bed-clothes and then flourished the knife as if it were a butcher's. When asked to indicate

the use of a pencil he wrote his name on paper; and when given a pair of scissors and asked to show how they should be used, he took them in his right hand and began to perform cutting movements clumsily, but, becoming dissatisfied, asked for a piece of paper saying, "I can't use these things without a something to cut."

When asked to show how to thread a needle, no needle being given, he carried out the necessary movements more successfully than when he actually held the needle and thread. When shown a key, and asked to indicate how this should be used, he went through the movements of inserting the key and unlocking a door in a more or less complete fashion. He was then given a closed padlock and key, and asked to use the key, whereupon, holding the lock in his right hand he fumbled with the key; eventually he succeeded in inserting the key into the hole, but even then was unable to unfasten the lock. When given a comb, and asked to show how it should be used, he clasped the comb tightly in the palm of his right hand, passed it into the palm of his left, worked it up to his fingers and immediately started to comb his hair by moving his head against the comb.

A lighted match was placed between the fingers and thumb of his right hand; as the match burnt he skilfully worked it up his fingers, and when nearly burnt blew out the flame.

When given a box of matches and a pipe loaded with tobacco, he placed the pipe in his mouth, held the box of matches clumsily in his right palm, opened the box with his left hand, took out three matches, discarded two of these, closed the box and then made several attempts to strike the box on the match; after several such movements the match lighted, whereupon he dropped the match box, transferred the lighted match to his right hand and carried it to his pipe, but in puffing at the pipe blew out the light. He then repeated the performance but could not light the pipe. After two attempts he remarked, "No, no, I can't do it, though I should like a smoke." When given the match already lighted he succeeded in lighting his pipe at the first attempt, and when asked to strike a match he did so readily.

When given a piece of string, and asked to tie a knot on it, he held the string tightly between the clenched fingers and palm of his left hand and attempted with his right hand to throw a loop and catch the string with his left index finger. In this manœuvre he made many attempts, but in each failed; eventually after trying five minutes he gave up, saying, "I know how to do it, I've tied so many in my time, I've been in so many kinds of business and in all I had to tie knots, but, you know, all my skill for such things has gone. Almost everything with my fingers I've lost most." At the same time he could distinguish and name most types of knots, e.g., sailor's, granny, reef, &c.

When given five pennies and a halfpenny and asked to count the money, he placed the coins in his left palm and, touching the pennies in turn with his right index finger, counted "One, two, three, four, five, five pence halfpenny, that's right, isn't it?" On being given two florins, a shilling and sixpence

he counted the money from his left hand into his right remarking, "Two, and two, and one, that is four, and three, and six, no, no, that is four and sixpence, that is five and sixpence, yes, yes, that is five and sixpence. I know that, that (the florin) is two shillings, and that, that is twice that (the shilling) and that is a sixpence." Given gold, silver and copper to the value of £3 4s. 11½d., he made several attempts to count it out, but could not give any result; when eventually told the amount he remarked, "Yes, yes, I know how much it is, you can't do me! but I can't tell you."

Five plates were placed on a table in front of the patient, and were audibly and slowly numbered 1, 2, 3, 4, 5, the exact plate being indicated with the finger as the number was called; on the table to the right of the plates were placed a penny, a sixpence, a florin, a half-crown, and a sovereign. He was then asked—

- | | |
|-----------------------------------|--|
| To put the sixpence on plate 5. | Performed. |
| To put the sovereign on plate 1. | At this he put the sovereign on plate 5, waited a moment, and then took it out and placed it on plate 1. |
| To put the half-crown on plate 1. | Performed. |
| To put the florin on plate 4. | Whereupon he put the florin on plate 1; when asked if this was right, he took sovereign from plate 1 and placed it on plate 4. |

When the test was made more complicated he usually paused and carried out a part of the command; on other occasions he would not attempt to perform any of the movements, although apparently he had understood, for he would remark, "I know what you say, and what I would like to do, but my hands seem all wrong." With practice on any one day the results obtained with this mode of testing became more and more accurate, provided that the orders were not made too complex, but on different days the accuracy of the results varied greatly. More accurate results were always obtained if the number given to the plates in front of him was written on them, provided that the numbers ran consecutively; if, on the other hand, the numbers on the plates were in the order, say, 5, 3, 4, 1, 2, the patient rarely succeeded in placing three of the coins consecutively on the desired plate.

When shown objects and asked to name them, he said when shown—

- | | |
|-----------------------|---|
| A pin. | (Readily) "pin." |
| A needle. | (Pause) "pin." |
| A pencil. | (Longer pause) "pin." |
| A watch. | "Half-past nine" (correct). |
| Yes, but what is it? | "Time piece." |
| Watch pocket in vest. | "Vest pocket." |
| The watch again. | (Readily) "vest-pocket holder"; he then became angry, shook his head and began to weep. |

A medicine bottle.

What does it contain?

A bunch of grapes.

But they are not made of
india-rubber, are they?

On being told that they were
grapes his face beamed, he
nodded and said—

A piece of string.

An electric light bulb.

A nail-brush.

The watch again.

A towel.

An inkstand.

A pocket-knife.

A fountain pen.

A pencil.

A pin.

"Bottle."

"My medicine."

(Long pause and then) "rubber balls."

After eating one he remarked, "I was driven to say rubber balls, oh, I know what they are; they are rubber balls and very good at that: yes, yes, very good rubber balls."

"I know that well enough, but words won't come, I can't think what they are."

"And very nice, too."

"String."

"Electric light bulb; yes, we make those at our works." (Words badly articulated.)

"Oval brush"; then he began to show how it should be used; as soon as the brush touched his finger nails, he remarked, "no, a nail-brush."

(Readily) "time piece."

(Pause, ten seconds) "towel," and then he read off the stamp, "London Hospital, Charrington Ward."

(Quickly) "inkstand."

"Knife, yes, pocket-knife."

"Penholder."

(Pause) "pen, no, fountain pen."

(Instantly) "pin."

When a pin was placed in his right hand and a needle was put into his left, and he was asked, What is the difference between a pin and a needle? he remarked "The two extremities of the one are sharp, the pin is sharp, one end is sharp, the other end is sharp, is blunt." The needle was then removed from his left hand, leaving the pin in his right, whereupon, pointing to the blunt end of the pin, he said, "Now that end is both sharp, one end I can put through it, it has got a sharp extremity, the other"—continuing to fumble with the pin—"now that end is both sharp, let me see, let me see, I know, no, I'm sorry, but I can't tell you." Given the needle into his left hand, whilst the observer held up the pin in front of him, he said, "That's better!" pointing to the point of the pin with his right hand, "That's a plain point," and pointing to the head of the pin, "That's dull and has no point at all." Then examining the needle in his left hand and pointing to the eye of the needle, "That has got a needle and a cotton goes through it, a needle has a

cotton to it." He was then given the pin and a length of cotton thread, whereupon he spent two minutes vainly attempting to pass the thread through the head of the pin, fumbling in a clumsy fashion and occasionally putting his left hand to his head as if in thought. At the end of this time he remarked, "No, no, let me see, let me see." On being given the needle and the thread, he said, "Now we're off," and spent two minutes more in vainly attempting to thread the needle, eventually giving up the attempt, saying: "My right hand is a fool, I can't use it at all."

The number of times the patient repeated any given action bore little or no relation to the accuracy of the performance of that action. Moreover, no improvement in the mode of carrying out the action could be obtained after showing him how to use objects placed in his hands. A movement once initiated, either voluntarily or in response to a command, could be continued after the closure of his eyes. Even with his eyes closed he was able to place his right upper extremity into any position into which his left had been placed either actively or passively. No differences between the accuracy of imitation of postures from right to left and from left to right could be determined. The hands partook normally in general movements of the body.

His ideas of objects seemed to be normal; he had knowledge of the desired results of actions which he wished to perform, of the parts of the body which he would have to move, and of the order of their movement in order to accomplish the desired action.

The general condition of the patient altered little during the first three weeks after his admission, but the interferences with speech, with the performance of purposive movements, and with memory varied considerably from day to day and from moment to moment. When the pains in his head were severe, his memory was less certain, and his ability in carrying out movements with objects and on command diminished. From examination to examination and during each examination the results obtained in answer to tests varied greatly, although the type of intellectual loss remained constant; the variations observed seemed to be determined by the amount of attention the patient was able to concentrate on the required thought or action; at times little or no loss appeared, at others the loss was great.

No actual loss of power and no definite paresis of any kind was discovered until September 5. On the night of the 4th to 5th the power in his left upper extremity diminished to such an extent that the grip on this side, measured on the dynamometer scale, fell in twenty-four hours from 80 to 30, whilst that of the right hand remained unchanged between 70 and 80. After this date he became more drowsy and heavy, and to testing less certain in his answers; at the same time the headache became more constant and more severe.

A radiographic negative of the skull taken on September 3 shows a loss of definition of the upper margins of the sella turcica, but no changes in the outlines of its floor or elsewhere in the skull, and no alteration in the density of the soft tissues of the cranium.

Gradually the weakness of the left upper extremity, first noticed on September 5, extended. On September 24 the patient was characteristically hemiplegic. The muscles of the left forearm and hand were absolutely flaccid and the patient was unable to move this extremity. He could not lift his left leg from the bed, but was just able to flex the knee and dorsiflex the ankle. The left leg was somewhat hypertonic and stiff. On the left side the knee-jerk and ankle-jerk, and to a less extent the deep reflexes of the arm, were exaggerated; ankle-clonus could not be obtained, but *both* plantar reflexes gave an extensor response. He could no longer control his sphincters.

Under observation the signs of disease in the chest gradually extended and before death affected the whole of the left lung; at the same time catarrhal signs appeared in the right lung. On September 22 the temperature became raised and irregular, and the rate of the pulse rose to 120 beats per minute; on the 28th the temperature reached 104° F., the pulse was uncountable at the wrist and the rate of respiration was 50 per minute. On the morning of the 29th, forty-four days after admission and eighty days after the onset of the squint, he died. An autopsy was performed on October 1.



AUTOPSY, OCTOBER 1, 1914.

Occupying the lower and posterior half of the lower lobe of the left lung was an ill-defined mass of carcinoma, measuring 6 cm. in diameter; the apex of the lower lobe also showed carcinomatous infiltration. A small secondary carcinomatous nodule was found in the centre of the lower lobe of the right lung. Secondary nodules of carcinoma, up to 3 cm. in diameter, were present in the glands at the hilum of the left lung and at the bifurcation of the

trachea; at the hilum of the right lung smaller secondaries were seen. The left lower paratracheal glands contained masses of secondary growth 2 cm. in diameter, and the right a mass measuring 4 by 2·5 cm., which was continuous with another mass, 7 by 4 cm., in the superior mediastinum. The left pulmonary vessels were constricted by these secondary glands. The lower end of the trachea and the commencement of the left bronchus were infiltrated by carcinoma, which had spread from the paratracheal glands. Masses of secondary carcinoma were also found in the right and left lower cervical glands, in the glands of the lower portion of the mediastinum and in the pancreatic glands. A secondary nodule measuring 6 by 5 cm. was found in the right suprarenal gland and a similar mass, 3 by 3·5 cm., was found in the left.

The brain weighed 1,439 grm. The meninges appeared normal. All the convolutions were flattened. The left supramarginal convolution contained a nodule of secondary carcinoma 2·5 cm. in diameter. This nodule was slightly adherent to the meninges, had a rounded form, and extended deeply into the subcortex. It was surrounded on its upper and anterior border by recent anæmic softening. The lower half of the post-central convolution was diffuent. The superior temporal, the angular, the upper part of the post-central, and the superior parietal gyri were unaffected, and no gross changes were seen in the other convolutions of the hemispheres. In macroscopical section the corpus callosum, the tapetum, and the inferior longitudinal bundle appeared normal.

The whole of the pituitary gland and the meninges around it were infiltrated with carcinomatous growth, which had eroded the floor of the sella turcica, and invaded, as a mass the size of a marble, the sphenoidal fissure.

In the medulla of the right femur, at the junction of its middle and lower thirds, an osteoplastic secondary nodule of carcinoma 1·3 cm. in diameter was discovered.

The upper part of the upper lobe of the left lung was collapsed and œdematous, whilst the lower lobe on the right side showed bronchopneumonic consolidation and mucopurulent bronchitis. Over both lungs a certain amount of serofibrinous pleurisy was discovered. The heart appeared normal; the liver and kidneys were congested, and the spleen was slightly enlarged and septic (weight 241 grm.).

Microscopic Examination.—Portions of (1) the left lung, (2) a lower cervical gland, (3) the left suprarenal, (4) the pituitary gland, and (5) the nodule in the left supramarginal convolution of the brain were embedded in paraffin; sections were stained by hæmatoxylin-eosin and van Gieson. The carcinoma is similar in appearance in all sections. It consists of tubules lined by columnar, cubical or polygonal cells, and less numerous, solid processes composed of polygonal cells. A little secretion is present in some tubules. There are areas of necrosis, which are infiltrated with numerous neutrophile leucocytes.

The pituitary gland is replaced by growth, with the exception of a narrow semilunar portion of the anterior lobe; in this remnant of the anterior lobe there are patches of necrosis.

The section of the brain includes half the rounded carcinomatous nodule and the convolution anterior thereto. The upper surface of the growth reaches the leptomeninges. The growth is confined to the supramarginal convolution; it is separated from the adjacent post-central convolution, in its upper part by a narrow strip of degenerate cortex, in its lower part only by leptomeninges in the intervening sulcus. The post-central convolution is oedematous, and many of its nerve-cells show considerable evidence of degeneration, for instance loss of angularity. The cortex opposite the lower part of the growth shows severe degeneration. In the anterior convolution there are no fat-granule cells.

For the notes on the autopsy I am indebted to Dr. Hubert Turnbull, Director of the Pathological Institute; my best thanks are also due to Dr. Lewis Smith under whose care the patient was admitted.

REFERENCES.

- [1] KLEIST. *Ergebnisse d. Neurol. und Psychiat.*, 1911, Band i, S. 343.
 - [2] KROLL. *Zeitschr. f. d. ges. Neurol. und Psychiat.*, 1910, Band ii, S. 315.
 - [3] LIEPMANN. *XVII Internat. Congress of Med.*, 1913, Section XI, Neuropathology, part ii, p. 97.
 - [4] VON STAUFFENBERG. *Zeitschr. f. d. ges. Neurol. und Psychiat.*, 1911, Band v, S. 434.
 - [5] STROHMAYER. *Deutsch. Zeitschr. f. Nervenheilk.*, 1903, Band xxiv, S. 372.
 - [6] WILSON, S. A. K. *Brain*, 1908, vol. xxxi, p. 164.
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A HITHERTO UNDIFFERENTIATED NUCLEUS IN THE FOREBRAIN (*NUCLEUS SUBPUTAMINALIS*).¹

BY GIUSEPPE AYALA, M.D.

Assistant Neurologist, Clinic of Nervous Diseases, Royal University of Rome.

IN this short communication it is desired to call attention to a somewhat important group of nerve-cells which have not been identified with any anatomical formation hitherto described. This formation was observed while studying the structure of the basal ganglia, especially the nucleus lenticularis, in the human brain and that of the monkey, by means of horizontal and frontal serial sections, stained by Nissl's method. Especial attention was paid to the surrounding structures connected more or less intimately with the nucleus itself. The most difficult of these formations to study, on account of the variability and irregularity of its arrangement as regards the nucleus lenticularis, is the substantia perforata anterior or lobus parolfactorius (Edinger). In this region, according to the work of Beccari [2], in all mammals, including man, we must distinguish: (a) a small anterior zone (eminencia parolfactoria), not always apparent in man, situated immediately behind the trigonum olfactorium; and (b) a large zona postero-lateralis (planum septale) in which there can be distinguished a more or less evident ridge, corresponding roughly to the diagonal bandlet of Broca, which is not always present in the human brain.

While studying the structure of the different formations of the substantia perforata anterior in man in relation to the overlying ganglion mass of the nucleus lenticularis, a group of nerve-cells of considerable size was observed which I shall call *nucleus hypolenticularis*, or more exactly, *nucleus subputaminalis*. An attempt to justify this appellation is given below.

In order to make clear the topographical position of this nucleus, it is well to remember some details of the external conformation of the ventral face of the nucleus lenticularis, and the various relations which

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this face has to the underlying structures. As is known, the ventral face of the nucleus lenticularis, at that point where the antero-ventral part of the putamen joins the head of the nucleus caudatus is crossed by a channel in which runs the lateral portion of the anterior commissure. This last, following a curved course in an oblique direction from interior to exterior, from front to back, and from above downwards, is submerged in the substantia perforata anterior and enters the above-mentioned channel. On this account the channel was called the canal of the commissura anterior by Gratiolet. Anteriorly the channel is situated between the ventral face of the head of the nucleus caudatus and the deep stratum of the pars anterior of the substantia perforata anterior, or more exactly, eminentia parolfactoria, in those brains in which the structure exists. The canal continues its course between the deep stratum of the planum septale and the ventral face of the nucleus lenticularis (which face is now formed by the putamen and the external segment of the globus pallidus), in such a way that the two segments of the nucleus lenticularis (ventrally) are separated from each other by the anterior commissure. Finally the commissure, crossing the inferior margin of the putamen at an acute angle reaches with its posterior extremity the lowest part of the external capsule and crosses the fibres of the fasciculus longitudinalis inferior. For this reason the ventral margin of the putamen is cut into two parts, one anterior, the other posterior. This is well shown in horizontal sections (somewhat obliquely inclined backwards) throughout the length of the lateral part of the anterior commissure. The anterior part, united with the head of the nucleus caudatus, extends distally like a beak external to the commissura anterior and internal to the lowest part of the capsula externa. The posterior part, on the contrary, remains interior to the commissura anterior, and exterior to the substantia perforata anterior and the substantia innominata of Reichert.

If we study the connexions of the ventral face of the nucleus lenticularis in vertico-transversal serial sections, it is seen that they change as we go from front to back. In fact, in front, in that plane in which the nucleus lenticularis is represented only by the anterior portion of the putamen, closely connected with the head of the nucleus caudatus, the ventral face of the nucleus lenticularis lies on the eminentia parolfactoria, and almost reaches the surface of the brain. More distally, on the contrary, that is to say as soon as we reach the plane in which the external segment of the globus pallidus appears, the ventral face of the nucleus lenticularis corresponds to the planum septale, from which it

is incompletely separated by the fibres of the commissura anterior and those of the ansa lenticularis.

We now note the appearance of the nucleus subputaminalis in the vertico-transverse and horizontal sections stained by Nissl's method. It is to be remembered that these sections must be cut strictly serially, i.e., it is necessary to stain all the sections of the series, otherwise the group of cells below described will be overlooked.

The nucleus subputaminalis begins to appear in the section passing through the level of the median part of the commissura anterior, namely, where the nucleus lenticularis is formed by the putamen and the external segment of the globus pallidus. Here the putamen is not well marked off ventrally from the deep stratum of the substantia perforata anterior (planum septale) and from the ventro-medial expansion of the claustrum. In this complicated and poorly determined zone (fig. 1) appears a small group of large nerve-cells, staining deeply with toluidin blue. These cells are elongated in shape. In the transversal direction, for the distance of about 1 mm., the group is in contact dorsally with the ventral margin of the putamen, the grey matter of which partly surrounds the medial apex of the group. In the photomicrograph the group of cells appears interrupted by a small blood-vessel.

Slightly distally, in the transverse section, at the level of the anterior part of the tuber cinereum, the ventral face of the putamen is still not well distinguished from the ventro-medial prolongation of the claustrum and from the grey mass which is below and behind, continuous with the nucleus amygdalæ. Here the cells of the nucleus subputaminalis appear slightly displaced to the outer side, in comparison with the previously mentioned section, and are larger in the transversal sense. It remains transversely in contact with the ventral margin of the putamen, except for a few fibres which probably belong to the capsula externa. The nucleus subputaminalis at this level (fig. 2) is of irregular shape and composed of a principal group of nerve-cells (fig. 2, a) and a small lateral group (fig. 2, b) united to the former by a few cells which are morphologically identical with those of the two groups. In all, the nucleus subputaminalis extends for 2 or 3 mm. transversely and for about 0.5 mm. vertically. All the cells composing the group are large and closely approximated (more so than in the preceding section) and in all cases stain deeply with toluidin blue.

In order to make the morphology and topography of the nucleus clear, a semi-schematic figure is given of a frontal section cut in a plane somewhat posterior to the one above described, i.e., at the level of the

infundibulum (fig. 3). The ventral face of the putamen is well separated in this section from the claustrum and substantia perforata anterior, by the lateral part of the commissura anterior. Externally

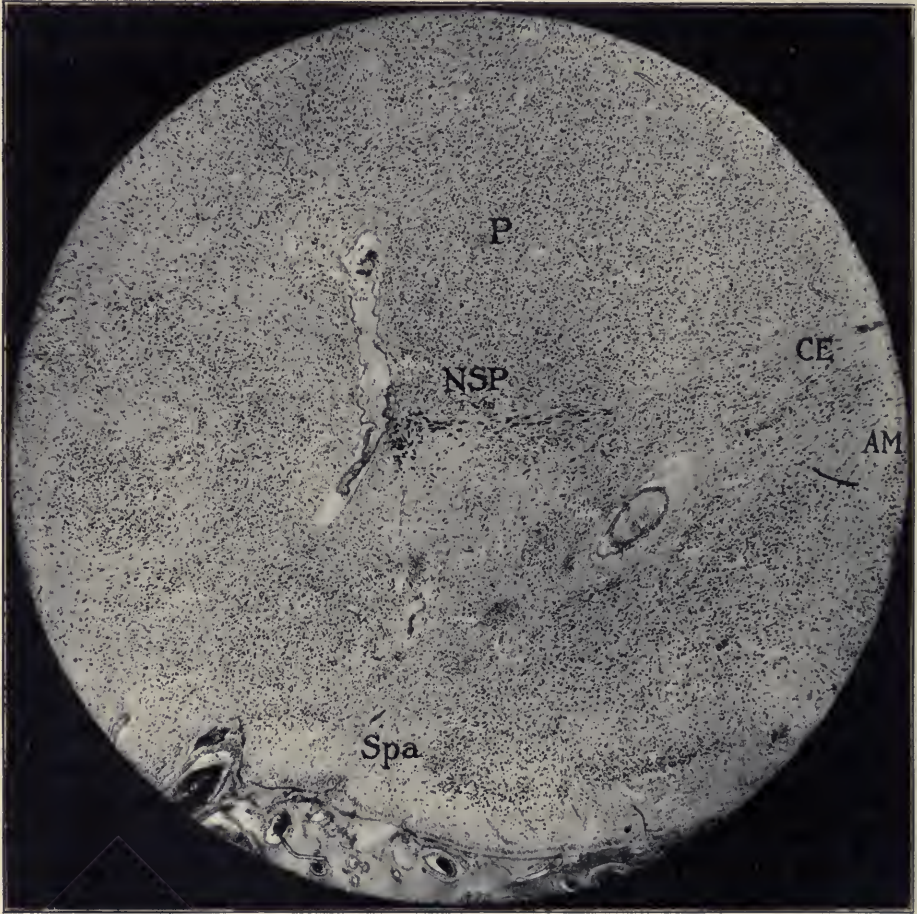


FIG. 1.—Photomicrograph from a frontal section of the right hemisphere at the level of the portio media of the commissura anterior. The proximal part of the nucleus subputaminalis is seen. AM = claustrum; CE = capsula externa; P = putamen; Spa = substantia perforata anterior.

to the commissura anterior, the nucleus subputaminalis is seen. It consists of large cells and extends transversely 3 or 4 mm. immediately below the ventral margin of the putamen. At this point the nucleus [seen better in the photomicrograph (fig. 4) than in the diagram] is

composed of a considerable group of cells lying transversely and extending medially as a prolongation, which, going upward and internally, enters into the angle formed by the ventral margin of the putamen and the

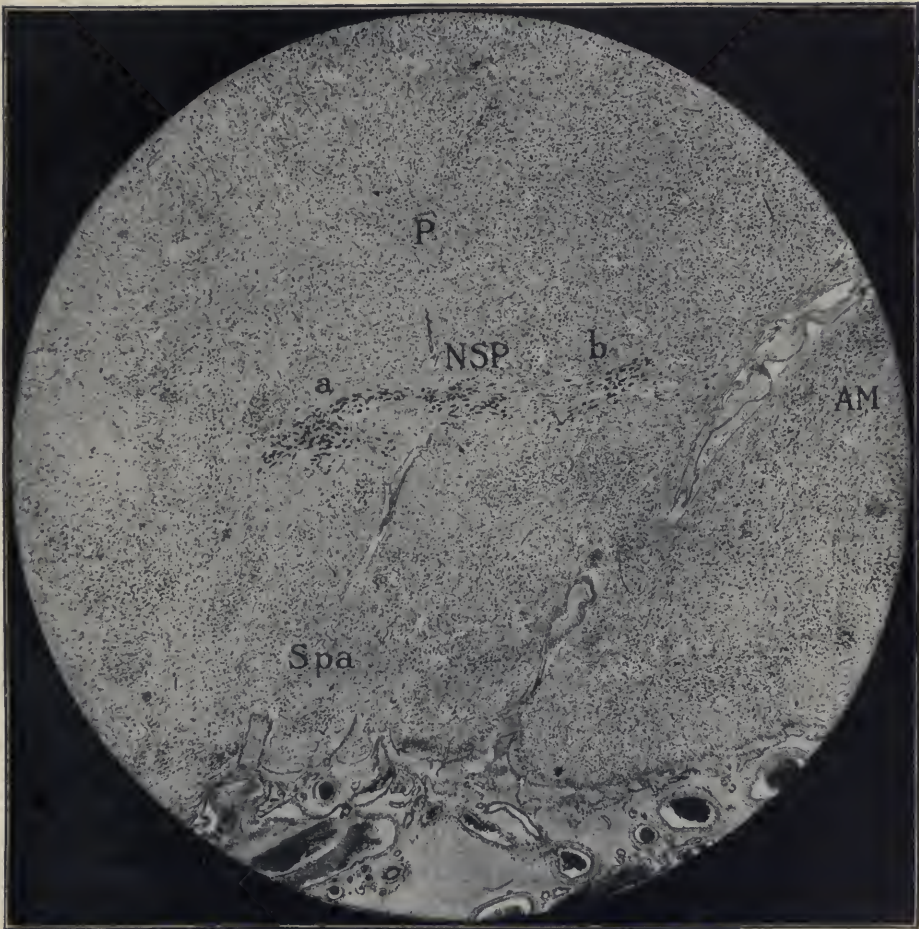


FIG. 2.—Photomicrograph from a frontal section of the right hemisphere at the level of the pars anterior of the tuber cinereum. The nucleus subputaminalis (NSP) is formed by two groups of cells—one medial (a), and the other lateral (b). Other lettering as in fig. 1.

external margin of the anterior commissura. Internal to the commissure, in the deep stratum of the substantia perforata anterior (planum septale) we can see another group of cells of medium size and sparse arrangement. This group extends laterally between the ventral part

of the globus pallidus and the commissura anterior, and is nothing else than the ganglion of the ansa peduncularis (Meynert [5]); nucleus basalis of Meynert (Kölliker [4]); nucleus of the planum septale (Beccari [2]); or ganglion of the ansa lenticularis (Edinger [3]).

In more distal frontal sections, the nucleus subputaminalis assumes a more lateral position and remains external and posterior to the external and posterior limits of the substantia perforata anterior. In the section immediately anterior to the corpus mammillare [fig. 5], we see that only the medial extremity of the nucleus subputaminalis remains. This extremity continues upward and inward with the prolongation, as in the preceding section. From its ventro-medial

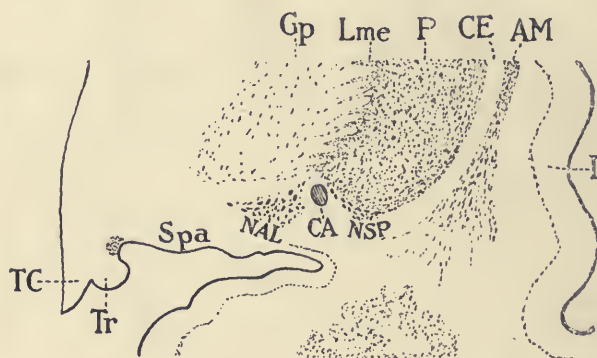


FIG. 3.—Semischematic figure (4 x 1) of a frontal section at the level of the tuber cinereum. Nissl stain—AM = claustrum; CA = commissura anterior; CE = capsula externa; Gp = globus pallidus; I = insula; Lme = lamina medullaris externa nuclei lentiformis; NAL = nucleus ansa lenticularis; NSP = nucleus subputaminalis; P = putamen; Spa = substantia perforata anterior; TC = tuber cinereum; Tr = tractus.

part some nerve-cells extend toward the nucleus ansa lenticularis. This last, however, remains internal to and below the commissura anterior and completely separated from the nucleus subputaminalis. As we gradually proceed distally, the group of cells, representing the medial extremity of the nucleus subputaminalis and its medial prolongation, gradually disappears.

In order to understand better the topography of the nucleus, it is necessary to study horizontal sections cut parallel to the orbital face of the lobus frontalis and, consequently, to the substantia perforata anterior. It is evident that, as shown by the frontal sections just discussed, the nucleus subputaminalis will not appear until we reach a section passing exactly through the level of the ventral face of the globus pallidus, i.e.,

a section in which, of the nucleus lenticularis, there exists only the ventral portion of the putamen, united anteriorly with the ventral portion of the nucleus caudatus. Proceeding from above downwards in the horizontal sections, the first appearance of the nucleus subputaminalis is the distal extremity which is a group of large cells situated exterior to the surface of the section of the lateral portion of the commissura anterior and internal to the ventral margin of the putamen. Distally this group of cells sends a prolongation back of the commissura anterior, thus coming in contact with the cells of the nucleus ansa lenticularis. This last remains entirely internal to the commissura, situated in the deep stratum of the planum septale. Although in the Nissl preparations of this level it is not possible to draw a sharp line between the nuclei, nevertheless the arrangement and morphology of the cellular elements indicate clearly enough where the one ends and the other begins. Certainly the horizontal sections confirm what we have seen in the frontal sections, i.e., that distally the nucleus subputaminalis is continuous with the nucleus ansa lenticularis by means of little branches of cells passing dorsally to the commissura anterior.

In a more ventral horizontal section (fig. 6) we see the ventral part of the putamen divided into a proximal and distal segment by the external striate vessels cut transversely. The internal margin of the proximal part is continuous with the posterior margin of the head of the nucleus caudatus, so that together they describe a curve with an interior concavity. In this concavity the commissura anterior and the nucleus subputaminalis are situated. The latter remains, throughout almost all its length, in contact with the median margin of the putamen; not all its length, however, for its distal portion is not seen because it lies a few microns dorsally (seen in the section last described). Here also the visible part of the nucleus subputaminalis describes a curve with the concavity inward. Antero-posteriorly it extends proximally to the point at which the putamen joins the head of the nucleus caudatus, and distally as far as the lateral margin of the surface of the commissura anterior, or more exactly, as far as the portion of the commissure which crosses the inferior margin of the putamen. Interior to the nucleus subputaminalis we see another group of small cells which may be identified with a fragment of the ventral portion of the putamen. The fragment lies in this situation on account of the direction which the commissura anterior takes at this point, where it crosses the above-mentioned channel. Thus the nucleus subputaminalis appears delimited laterally and frontally by the internal margin of the

putamen, and medially by a fragment of the putamen and commissura anterior which separate it from the nucleus ansa lenticularis. The details and arrangement of the nucleus are more evident in the photomicrograph (fig. 7), corresponding to the semi-schematic fig. 6. In

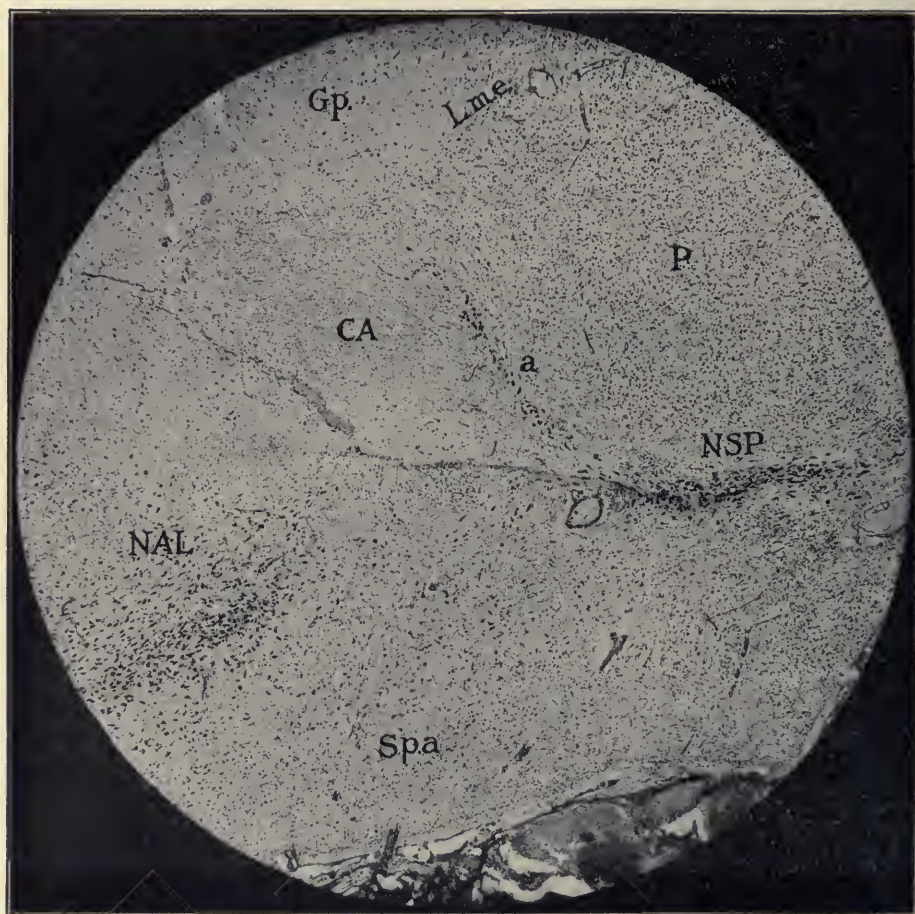


FIG. 4.—Photomicrograph from frontal section of right hemisphere at the level of the infundibulum. Medially from the nucleus subputaminalis a prolongation (a) is directed upward and medially between the putamen (P) and the commissura anterior (CA). Other lettering as in fig. 3.

the photomicrograph the nucleus subputaminalis appears of very irregular shape, inasmuch as the antero-median extremity is circumscribed, while in the median portion it becomes larger, then smaller and finally large again, till it reaches the vasa striata, which interrupt

it abruptly. Interior to the nucleus and in front of the superficial section of the commissura anterior, we see the fragment of the ventral portion of the putamen. Still more interiorly, as regards this last fragment and the commissura anterior, we can see some sparsely

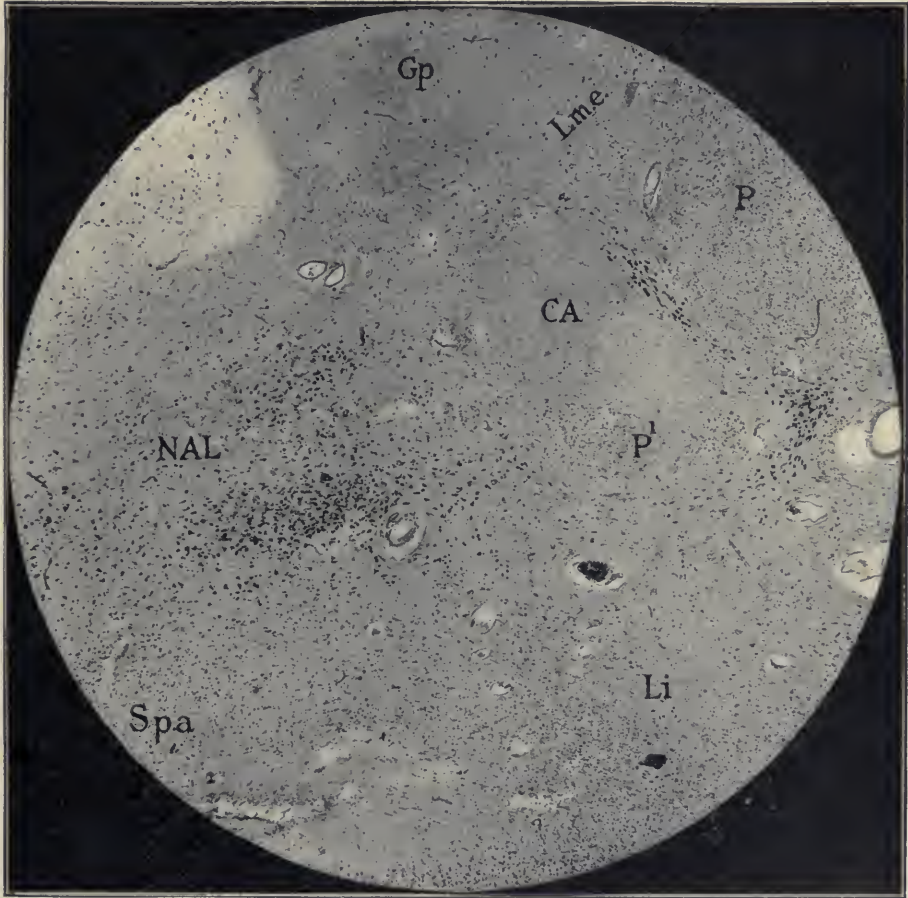


FIG. 5.—Photomicrograph of frontal section of right hemisphere immediately in front of the tuberculi mammillari. The nucleus ansa lenticularis (NAL) is enlarged, and remains clearly separated from the nucleus subputaminalis (NSP) by the commissura anterior (CA) and a fragment of the putamen (P'). The nucleus subputaminalis is reduced to a group of cells situated outside the substantia perforata anterior (Spa), corresponding to the limen insulae (Li). Other lettering as in fig. 3.

arranged nerve-cells. These are nothing else than the lateral portion of the nucleus ansa lenticularis. Anteriorly and exterior to the nucleus subputaminalis, we see the ganglion mass belonging to the

proximal part of the ventral margin of the putamen. The same photomicrograph shows the disposition of the cells of the various segments of the nucleus subputaminalis. Here, although irregularly distributed, the cells are in general closely approximated, and it is not possible to differentiate the individual cells with the low power objective. The cells of the nucleus ansa lenticularis, as has been mentioned, are, on the contrary, in more or less dense groups which, although also irregular in arrangement, are always clearly separated from one another.

Proceeding vertically by means of horizontal sections, the nucleus subputaminalis disappears altogether.

At this point, it is best to explain that the appearance noticed in the above-mentioned frontal and horizontal sections is not constant, and in certain other sections assumes a different form. The reason for this variation is (1) because the nucleus does not lie exactly in a horizontal plane, and (2) because it describes a curve in the antero-posterior direction. Besides the disposition of the nucleus differs somewhat in the two hemispheres, for, adapting itself to the ventral margin of the putamen and following the individual variations in the form and direction of the latter, it necessarily varies with it. Nevertheless, in the horizontal sections the nucleus subputaminalis, on the whole, describes a curve with the concavity internal and posterior. It is larger in its median part than in the proximal and distal extremities, as shown in the vertical transverse sections.

Resuming the description of the horizontal and frontal sections, we can say that the nucleus subputaminalis is a dense group of cells situated beneath the ventral portion of the putamen (*portio media*), at the point where this margin is crossed by the *commissura anterior*. Although its contour is somewhat irregular, as a whole it is flat in the vertical and curved in the horizontal plane. The direction of its greater axis is oblique, passing from the exterior inward and from front to back. It extends antero-posteriorly for about 1 cm. from a frontal plane which passes through the median part of the *commissura anterior* to another frontal plane passing immediately in front of the *corpus mamillare*. Transversely it measures at its greatest length at least 2 or 3 mm. It is bounded (*a*) dorsally by the inferior margin of the putamen, from which it remains separated by some ventral fibres of the *capsula externa*; (*b*) internally, in part (distally), by the *commissura anterior*, and in part (proximally) by a fragment of the putamen which surrounds its medial extremity; (*c*) ventrally and externally by fibres of the *capsula externa*, and distally by the complex ganglion mass which constitutes the *limen insulæ*.

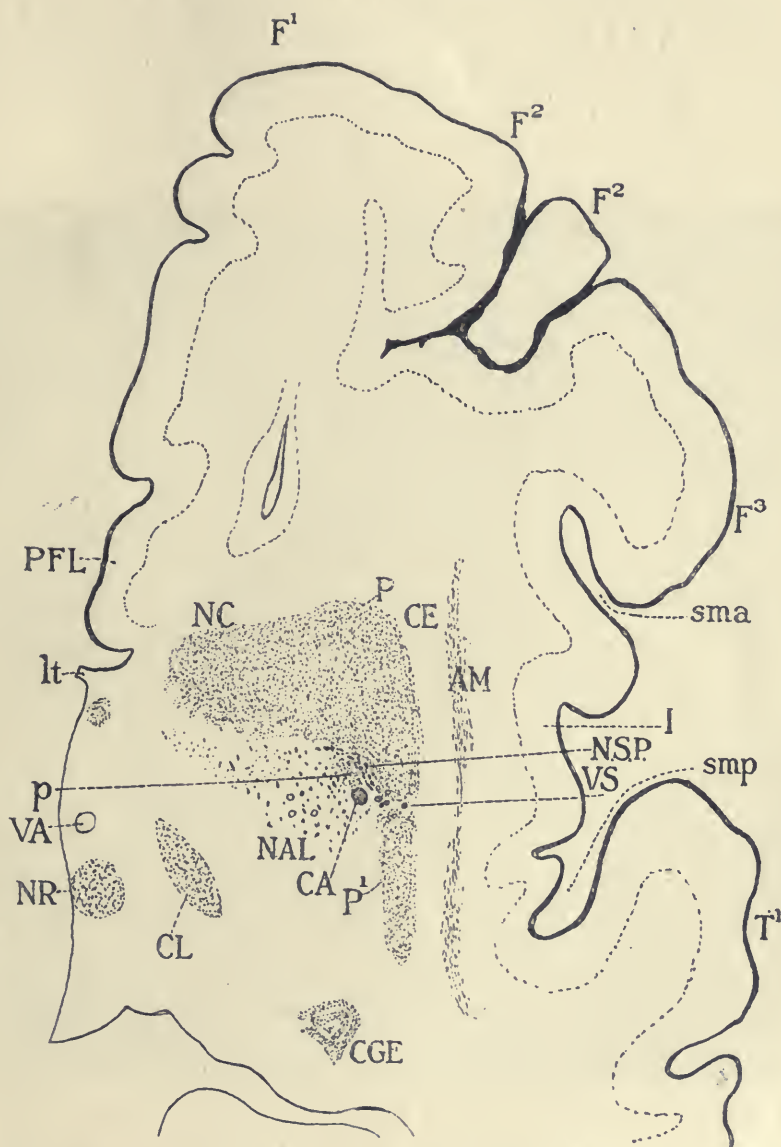


FIG. 6.—Semischematic figure (4 x 1) of a horizontal section parallel to the ventral face of the globus pallidus, immediately below the ansa lenticularis. CL = corpus luyisii; CGL = corpus geniculatum lateralis; F¹ F² F³ = gyri frontales; lt = lamina terminalis; NC = nucleus caudatus; NR = nucleus ruber; P = putamen (proximal extremity); P' = putamen (distal extremity); p = putamen (fragment of the ventral margin); PFL = area parolfactoria ("piega-fronto-olfatto-limbica"); sma = sulcus marginalis anter. insulae; smp = sulcus marginalis poster. insulae; T¹ = gyrus temporalis superior; VA = fasciculus thalamo-mammillaris; VS = arteria striata externa. Other lettering as in fig. 3.

The cells of the nucleus are easily distinguished in the Nissl preparations from the adjoining grey formation, by their morphology and structure (fig. 8). The most prevalent forms are oval, pyriform and sometimes fusiform. They measure in greatest diameter 40 to 50 microns. Many appear in frontal sections with the greater axis transverse.

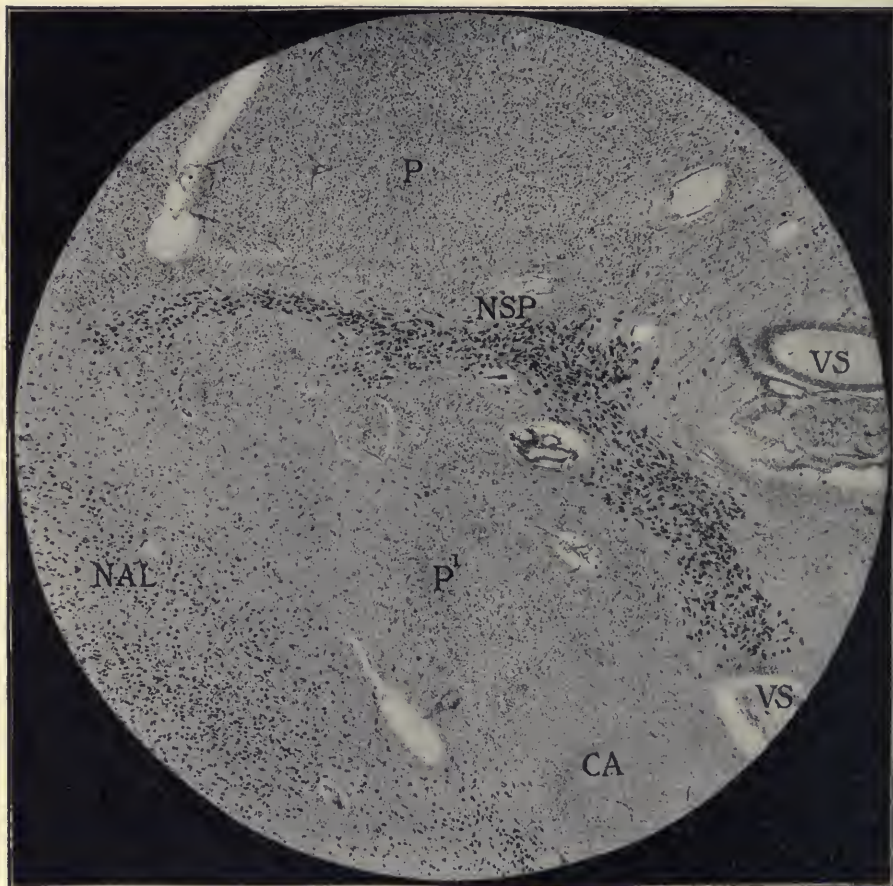


FIG. 7.—Photomicrograph of a horizontal section immediately below the ventral face of the globus pallidus. Lettering as in fig. 6.

The nucleus is of moderate size (12 to 14 microns), vesicular or ovoid in shape and somewhat poor in chromatin, and the situation is always excentric. There is a small, somewhat round, deeply staining nucleolus. The cytoplasm, which makes up a considerable part of the cellular body, is very rich in tigroid substance. This appears (*a*) in the form of large

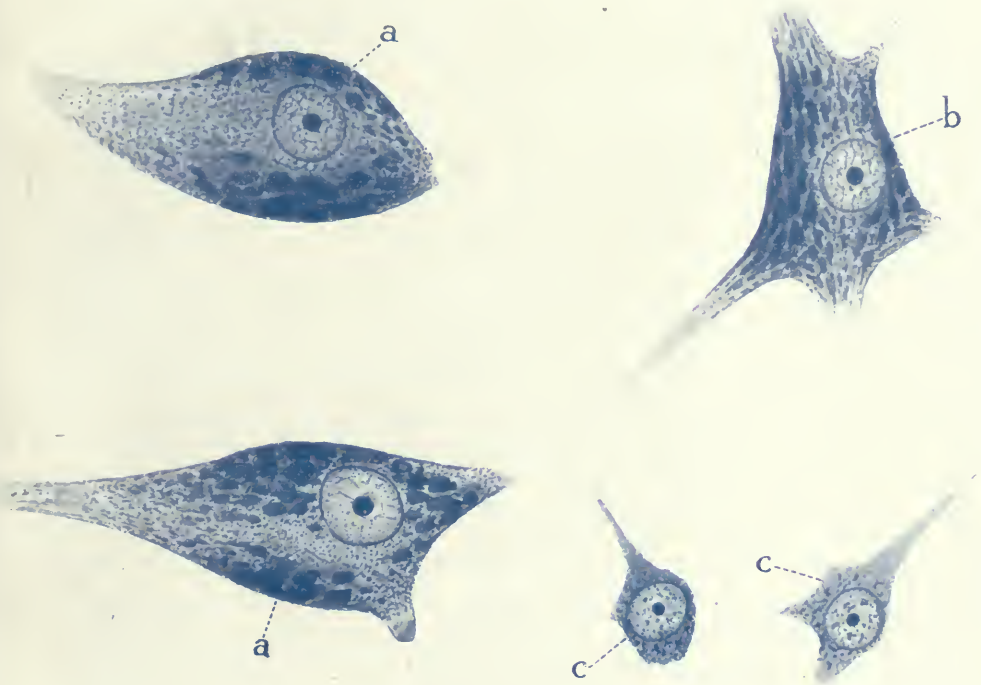


FIG. 8.

- a* = Nerve-cells of the nucleus subputaminalis.
b = Nerve-cell of the n. ansa lenticularis.
c = Nerve-cells (middle size) of the putamen.

Preparations from the brain of a patient dead of lobar pneumonia, fixed in alcohol and stained with toluidin blue. Drawn by artificial light. Objective $\frac{1}{2}$, ocular 6 (Leitz).



somewhat round masses, staining deeply with toluidin, and which, although irregularly distributed, are dense at the periphery, or at the two poles of those cells which are of elongated form; and (b) in the form of small granules staining more or less deeply and sparsely distributed throughout the cytoplasm. Both the masses and the granules of the tigroid substance are rarely continued into the dendrites, where they assume an elongated shape. A peculiarity of these cells is that they stain intensely with toluidin, thionin, methylene blue, &c., even in weak solutions. They retain their stain long after the rest of the section is almost discoloured by age.

It might be supposed that the nucleus above described represents a detached portion or appendix of some adjacent anatomical structure, from the fact that it is found near the putamen, the ventro-medial portion of the claustrum, the substantia perforata anterior, and the nucleus ansa lenticularis. This last is considered, by Beccari, a deep formation of the planum septale. The reasons for distinguishing the nucleus subputaminalis from the above structures are as follows. First of all, a glance at the sections or corresponding photomicrographs is sufficient to exclude the possibility of its belonging to the putamen or claustrum, partly because these two are clearly separated from it, and partly because the cells are absolutely different in size, form, and structure, from those of the nucleus subputaminalis. In fact the greater part of the cells of the putamen (shown in a former publication on the nucleus lenticularis [1], are small or of medium size (8 to 15 microns), inconstant in shape, and having a relatively large nucleus. The cells are poor in cytoplasm and chromatin granules. It is true that in the putamen there are some giant cells, but they are very rare, isolated, and well distinguished, on account of their size, polygonal shape and structure, from those of the nucleus subputaminalis. The cells of the claustrum, although a greater part are a little larger than those of the putamen, never reach the size of the cells of the nucleus subputaminalis. Their shape in this zone is, in general, fusiform. They are situated in the long axis vertical and almost parallel to the fibres of the capsula externa.

As regards the connexion of the nucleus subputaminalis with the substantia perforata anterior, it is first to be pointed out that the greater part of the nucleus subputaminalis is situated externally and behind the substantia perforata anterior, i.e., immediately above the point where this substance is continuous with the limen insulæ. Only a small part (proximally) corresponds to the deep stratum of the substantia perforata

anterior, or more exactly its external zone according to the division of Cajal [6], or to the planum septale, according to the division of Beccari [2]. Cajal, speaking of the external region of the substantia perforata anterior in man, describes four strata, three formed of cells and one of fibres. He does not mention a ganglion of large cells, situated and shaped as above described for the nucleus subputaminalis. In the deeper stratum of this region (stratum of fusiform and triangular cells) can be found in all cases, according to Cajal, certain other islets of cells widely separated from each other. These cells are giant, stellate, triangular, or fusiform in type. "They resemble," he says, "motor cells in shape and structure, as they possess an abundant protoplasm, rich in masses of chromatin and a great quantity of yellowish pigment." Evidently Cajal did not refer to a well defined formation, but rather to the cells of the nucleus ansa lenticularis which here and there appear irregularly grouped.

Even Beccari, in a most accurate description of the parolfactory region, describes in the planum septale (external region of the substantia perforata anterior of Cajal) two superficial strata of cells, and adds that the nucleus ansa lenticularis of Meynert, to which he gave the name of nucleus planum septale, is above them. He here follows the description of Kölliker. If this region is studied by means of Nissl's method of staining, it seems at first sight that the group of cells situated under the putamen is nothing more than the nucleus ansa lenticularis. However, if studied systematically in a complete series of horizontal and frontal serial sections, as pointed out above, one sees that it is a distinct formation, although distally connected with the nucleus ansa lenticularis. In fact the latter, as Kölliker and Beccari have shown, begins distally in the vicinity of the posterior extremity of the corpus mammillare, as a group of cells lying between the optic tract and the cauda of the commissura anterior, corresponding to the inferior extremity of the lamina medullaris externa of the nucleus lentiformis. This nucleus, covering the ventral face of the globus pallidus, extends frontally until some of its cells reach the posterior margin of the head of the nucleus caudatus. Although the nucleus ansa lenticularis extends, by means of prolongations, between the globus pallidus and the commissura anterior, there is no doubt that its body proper remains internal to the commissure, and below the ventral face of the globus pallidus, from which it is separated by means of the fibres of the ansa lenticularis. On the contrary, as we have seen, the nucleus subputaminalis is situated, as a whole, immediately external and slightly ventral to the commissura anterior (portio lateralis) and is approximated to and almost surrounded by the grey substance of the ventral margin of the putamen.

The reason for the distinction between this nucleus and that of the ansa lenticularis is that there exist certain structural and morphological differences between the elemental cells composing them. The cells of the nucleus ansa lenticularis are irregularly arranged and always widely separated from each other and form a more or less dense stratum which occupies the deep layer of the planum septale. On the other hand, the cells of the nucleus subputaminalis are densely and uniformly arranged and constitute a very compact group hardly distinguishable with the low-power objective. Still, the individual cells of the nucleus ansa lenticularis, although they are fairly large (20 to 30 microns according to Kölliker), and rich in chromatin, as are those of the nucleus subputaminalis (fig. 8b), in general, are of smaller size, since those of the latter measure 40 to 50 microns. While the shape of the cells of the nucleus ansa lenticularis is multipolar and polymorphous, that of the cells of the nucleus subputaminalis is elongated, oval, or pyriform. Finally, the structure of the two groups of cells appears somewhat different inasmuch as the tigroid substance of the cells of the nucleus subputaminalis occurs in the form of small granules or large masses disposed usually at the periphery of the cells, while in the cells of the nucleus ansa lenticularis the chromatin masses are smaller and irregularly distributed.

For the above reason it seems justifiable, from a descriptive point of view, to differentiate the one from the other, and to individualize the nucleus subputaminalis as a distinct anatomical formation. It is here intended by the term "nucleus subputaminalis" simply to indicate the topographical situation and to leave open the question of its morphological significance and functional value. Nevertheless, it seems highly probable that the nucleus subputaminalis and the nucleus ansa lenticularis, which might be called *nuclei hypolenticulares*, are, from the point of view of general morphology, formations which bear the same relation to each other as the putamen and nucleus caudatus.

The nucleus above described in man was found well developed in some monkeys in which, although smaller than in man, it preserves its characteristic position under the putamen, and is always distinct from the nucleus ansa lenticularis.

GENERAL EXPLANATION OF FIGURES.

The photomicrographs and semi-schematic figures are taken from frontal and horizontal serial sections, fixed in alcohol and stained with toluidin blue. The block, from which the sections are cut, includes all

the basal ganglia. The photomicrographs are all of the same enlargement and show the nucleus subputaminalis and the surrounding structures.

BIBLIOGRAPHY.

- [1] AYALA, G. "Il nucleo lenticolare dal punto dirista anatomico," Roma, 1914.
 - [2] BECCARI, N. "La sostanza perforata anteriore e i suoi rapporti col rinencefalo nel cervello dell' uomo," *Arch. Ital. di Anat. e di Embriol.*, 1911, vol. x, p. 261.
 - [3] EDINGER. "Vorlesungen über den Bau der nervösen Zentralorgane des Menschen und der Tiere," 8 Aufl., Leipzig, 1911.
 - [4] KÖLLIKER. "Lehrbuch der Gewebelehre des Menschen," 1896, Bd. ii, S. 456.
 - [5] MEYNERT. "Vom Gehirn der Säugethiere," in Stricker's "Handb. der Lehre von den Geweben," 1872, S. 694.
 - [6] RAMÓN Y CAJAL. "Histologie du système nerveux de l'homme et des vertébrés," Paris, 1909, tome ii, p. 727.
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PUBLICATIONS RECENTLY RECEIVED.

[Notes on a book under this heading do not preclude a subsequent review.]

Die Lokalisation im Grosshirn. Von Professor C. v. MONAKOW
S. 1033. Mit 268 Abbildungen im Text und 2 Tafeln. Wiesbaden: Bergmann, 1914.

Von Monakow has always been strongly opposed to the current views on cortical localization. In this book of over a thousand pages, he has considered every aspect of the question, summing up his ideas on the subject at the end of each section.

The key to von Monakow's position is an understanding of the process he has called "diaschisis." Although it is one of the accompaniments of surgical shock, the two conditions are in no sense the same; diaschisis is a cessation of function starting from the local lesion and extending to normal portions of the grey matter which receive fibres from the injured part. This is not primarily a loss of function following physiological lines, but is a nutritional change following a strictly anatomical distribution. The effect of the lesion "cleaves through" neuronal junctions, so that the loss of function attacks parts belonging to distant neuronal systems, which, however, are connected normally with the part affected. Thus, for instance, a cortical ablation may cause a loss of motor power corresponding to that due to lesions of the anterior horn-cells, or hemianalgesia resembling that seen in lesions of the mid-brain.

It is at once obvious that, on this view, the ordinary conceptions of cortical localization are erroneous, and the evidence on which it is based fallacious. Von Monakow, therefore, begins by considering how function returns after an experimental lesion, and points out the long duration of diaschisis. He then considers, one after the other, the various methods used to prove the existence of motor and sensory centres in the cortex.

These are (1) extirpation and examination of the subsequent loss of function; (2) physiological excitation; (3) anatomical methods, including the study of the cyto-architecture; (4) the method of comparative anatomy; and lastly (5) the clinical anatomical method.

The usual conception of a motor centre is a localized area from which single definite movements can be evoked, in some part of the opposite half of the body, by local stimulation; at the same time removal of this area should cause paralysis in that part. But, according to von Monakow, these "centres" are not the places where voluntary movements are manufactured, but nodal points for the production of synergic movement out of a host of motor impulses, called into activity for the most part reflexly. Destroy these points and the

only specific effect is the diminution of co-ordination and synergy, although the immediate consequence is the production of a gross paralysis by diaschisis. Thus he believes that all the physiological evidence deduced from ablation and stimulation is fallacious, provided it is used to prove the localization of the lost function or the movements following excitation in that part of the cortex.

He also believes with Brodman that cyto-architecture is no clue to function, instancing the absence of large pyramidal cells from that area of the cortex where movements can be excited in the arm. Moreover, he thinks that no anatomical motor area can be proved to exist even in the monkey by ablation of the cortex and subsequent study of degeneration of the pyramidal tracts.

He sums up his views on localization of movement on p. 215; there is, he believes, a cortical somatic zone, but this is simply the spot of most complete representation of movement ("Optimale anatomische Repräsentationsbezirke"). Any movement evoked by the will demands the activity of a host of other centres, not only lower in the nervous system, but also in other parts of the cortex. This simultaneous working of centres at various levels of the nervous system in many ways closely resembles the views of Hughlings Jackson, which seem to be unknown to von Monakow.

He then considers the localisation of sensibility, and here we think the German method of talking about "bewusste und unbewusste Sensibilität" for processes in the spinal cord and mid-brain militates against clearness of exposition and thought. Sensation is a mental process, and the English terms "sensory and non-sensory afferent impulses" would have rendered von Monakow's handling of this part of his work considerably clearer. Both central convolutions take part, he thinks, in the building up of "sensory stimuli" flowing to them from the periphery.

Stereognosis is the subject of special consideration, and he believes it is a "gnostic" act; its loss is an "agnosia" depending on many special sensory impulses. These only can be said to be susceptible of anatomical localization in the cortex.

He then considers the cortical affections of vision, the question of visual agnosia and mind-blindness, and denies that any of these conditions are permanent phenomena invariably caused by one localizable anatomical defect, or that they are due to removal of a "centre for visual images."

The seventh chapter is devoted to apraxia, and here von Monakow is diametrically opposed to Liepmann. He believes that apraxia is a complicated group of symptoms and possesses no anatomical localization beyond that of its components. Unilateral apraxia is always associated with gross changes such as paresis or disturbance of "deep sensibility"; bilateral apraxia is accompanied by agnosia or aphasia. Next, he deals with aphasia in the same way. Here he is profoundly influenced by Semon's theory of memory, and the idea that the underlying physical basis of memory depends on "engrams." The most valuable part of this chapter is an analysis of the anatomical conditions found in all the published cases which came to autopsy; these are arranged in groups, accompanied by admirable diagrams. The book closes with a short account of the problem of the localization of mental activities in the frontal lobes.

However much he may disagree with von Monakow's views on cerebral localization, no one, in future, can consider the subject without careful study of the enormous material contained in this book. The diagrams and illustrations are numerous and beautifully executed.

Localisations Cérébelleuses. Par ANDRÉ THOMAS et A. DURUPT. Pp. 197, avec 92 Figures dans le Texte. Paris: Vigot Frères, 1914.

These authors have long occupied themselves with the functions of the cerebellum, and have made several communications on their researches to the Société de Neurologie. The present work is a complete account of their experiments, and the views they now hold on the localization of function in the cerebellum. Any loss of function due to local lesions has the following characters: (1) Active movement is disturbed, impulsion is excessive and too rapid, cessation too slow (dysmetria); (2) it is possible to change the movement of the affected limbs passively, and to place them in various positions without the animal attempting to resist or readjust them; (3) excessive reaction when the limbs are forced into certain positions opposed to those assumed passively; (4) the absence of reaction which should normally occur to certain excitations arriving from the joints.

In how far can it be said that local lesions produce these changes in any one or other part of the body? The authors conclude that distinct centres exist in the cerebellar hemisphere for the upper and lower limbs (for details consult p. 142). Each of these centres can be divided into secondary ones corresponding to a segment of a limb or one articulation. Each presides over movement in a certain direction, and is "hyposthenic" for the muscles which carry it out, but "hypersthenic" for their antagonists. These centres can be called into action by conditions which alter the posture of the limbs, and are responsible for the maintenance of static tone. Any loss of function in one of these centres disturbs the equilibrium of the limb, and thus diminishes the accuracy of movement. Hence dysmetria, adiadococinesia, and other motor troubles found in disease of the cerebellum. Conscious sensations are never affected; the change is a want of reaction to unconscious articular and static afferent impulses. The cerebral cortex remains dominant and tends to supply, to a greater or less extent, the function diminished by the lesion of the cerebellum; but although recovery may appear to be complete, fear or anything which distracts attention will bring out the previous loss of function in the affected limb.

The Brain in Health and Disease. By JOSEPH SHAW BOLTON, M.D., D.Sc., Medical Director West Riding Asylum, &c. Pp. 479, with 99 Illustrations. London: Arnold, 1914.

Dr. Bolton was one of the first to describe the cyto-architecture of the cerebral cortex, and his work on the visual area is well known. The first part of this book, devoted to the minute structure and development of certain

parts of the cortex, contains the fruit of a large amount of individual research. This is followed by an attempt to determine the localization of function in anatomical structures of the cortex; "visuo-sensory," "visuo-psychic," and "psycho-motor" zones are described, and the prefrontal area is held to be the "voluntary-cerebral-associative region." A chapter is devoted to language and thought, and another to feeling, emotion and sentiment; these contain less personal observation.

The second half of the book is devoted to the author's views on cerebral function in mental disease, and the abnormal appearances of the cortex found in the insane. He considers that the brains of some patients show obvious want of development in certain layers, whilst in other cases the deficiency in depth was due to disease. All mental disease is therefore divisible into two groups, "amentia," and "dementia," according to whether the fault is due to want of development or disease. This leads to a somewhat unusual classification of mental disease, of which many examples are analysed from the author's standpoint. The illustrations are extremely good.

An Introduction to the Study of Colour Vision. By J. HERBERT PARSONS, D.Sc., F.R.C.S. Pp. 308, with 75 Figures. Cambridge: University Press, 1915.

At a time when there is much loose writing on the subject of theories of colour vision, this book will come as a valuable reminder of the difficulty of the problem and the great labour expended on attempts at its solution by many devoted workers. Dr. Parsons has attempted to indicate what we know of colour vision from its physical, physiological, and psychological aspects. He shows a profound knowledge of the literature of the subject, and the references he gives to the source of every statement made would alone make his book a valuable addition. After a short introduction he describes the spectrum as seen first by the light-adapted eye, and then by the dark-adapted eye; this opens up the question of luminosity and colour mixture. The fields of vision for colour are given, and he then passes to a consideration of simultaneous and successive contrasts with the phenomena of flicker and fatigue.

Part II is devoted to the facts of colour blindness, and Part III to the chief theories of colour vision. It is impossible for anyone to approach this subject without some predilection to some one or other aspect of the controversy. But, whatever views the author holds, he has succeeded in stating the main theories, and the results of the work based upon them, in a singularly clear light. From his account and from the references he gives, anyone is placed in the position to follow up any of the principal hypotheses. Hering said, "Sterile theories easily relinquish immortality. Fruitful theories hand down their immortal part to their children, whilst their ephemeral shell falls to pieces." Dr. Parsons has indicated the observations upon which each of the great theories has been built up, and shown where knowledge has advanced though hypotheses fail.

Feeble-mindedness, its Causes and Consequences. By HENRY HERBERT GODDARD, Ph.D. Pp. 599. Illustrated by a large number of photographs. New York: Macmillan, 1914.

The author of this book is the Director of the Research Laboratory of the Training School at Vineland, New Jersey, and in this capacity he applied the Binet tests to a large number of feeble-minded girls and boys. In each case an attempt was made to obtain as complete a pedigree as possible of each patient with the help of trained workers, and the larger part of the book is made up of these pedigrees with a short description of the patient's mental and physical condition, illustrated in most cases by photographs. In exactly half the author's cases the feeble-mindedness was hereditary, and in half these patients both parents were feeble-minded. Alcoholic excess, syphilis, illegitimacy and all forms of mental defect were present in enormous excess in these families, and the author is almost inclined to look upon feeble-mindedness as a "unit" character from the hereditary point of view. By no means all cases of mental defect arise from a defective stock: some seem to be sports in a normal family, whilst a larger proportion of the non-hereditary cases are the direct consequence of some infantile disease such as cerebro-spinal meningitis. In the introductory and concluding chapters the conclusions, though dogmatically expressed, are of great general interest, and give a fair idea of the social problems opened up by such work.

Mentally Defective Children. By ALFRED BINET and TH. SIMON. Authorized Translation by W. B. DRUMMOND, M.B., C.M., F.R.C.P., with an Appendix containing the Binet-Simon tests of intelligence, by MARGARET DRUMMOND, M.A. Pp. 180. London: Arnold, 1914.

This is a translation of Binet and Simon's account of how they came to institute their tests for defective intelligence. In places it deals almost entirely with French conditions, and vivacious accounts are given of the difficulties which met them in their campaign for reform. The most useful portion of the book at the present time is the complete list of the tests and a guide to the method of carrying them out.

Syphilis and the Nervous System. By Dr. MAX NONNE. Authorized Translation from the second revised and enlarged German Edition by CHARLES R. BALL, M.D. Pp. 406, with 98 illustrations in the text. Philadelphia and London: Lippincott. No date.

This is a somewhat abbreviated translation of the second German Edition of Nonne's well-known book: it contains all the excellent photographs and diagrams of the original, and strictly follows its readable arrangement. Many of the brilliant little clinical descriptions of cases have been omitted, but the others have been incorporated in the text.

The Intervertebral Foramen, an Atlas and Histologic Description of an Intervertebral Foramen and its Adjacent Parts. By HAROLD SWANBERG. Pp. 101, illustrated by 16 full-page plates. Chicago: Scientific Publishing Company. No date.

The purpose of this little book is to present an accurate description of the right first dorsal intervertebral foramen and its contents in the cat. One specimen only was examined, and the foramen and its contents were cut into sixty sections; but as the nervous structures were not stained differentially no new facts appear from this curious piece of work.

Mental Diseases: A Text-book of Psychiatry for Medical Students and Practitioners. By R. H. COLE, M.D., M.R.C.P. Pp. 353, with 52 illustrations and plates. London: Hodder and Stoughton, 1913.

This text-book will be useful to the student who wants an introduction to the study of insanity. It follows clinical lines, and deals shortly with all the common forms he is likely to meet. The photographs of patients are unusually good, and the final chapters on prognosis and the law of lunacy and mental deficiency are the best in the book.

Orthopædics in Medical Practice. By Professor ADOLF LORENZ and Dr. ALFRED SAXL. Authorized Translation from the German by L. C. PEEL RITCHIE, M.D., F.R.C.S., Ch.M. Pp. 288, with 39 illustrations. London: Bale, Sons and Danielsson, 1913.

This is a good translation carried out by a surgeon who was a voluntary assistant in Professor Lorenz's clinic. The great mass of the book deals with the rectification of deformities and disabilities due to disease of the nervous system; yet its feeblest side is the neurological. The time has past when any surgeon who is not fully imbued with the ideas of modern neurology can hope to write successfully on such a subject.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I. to XXIII. inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

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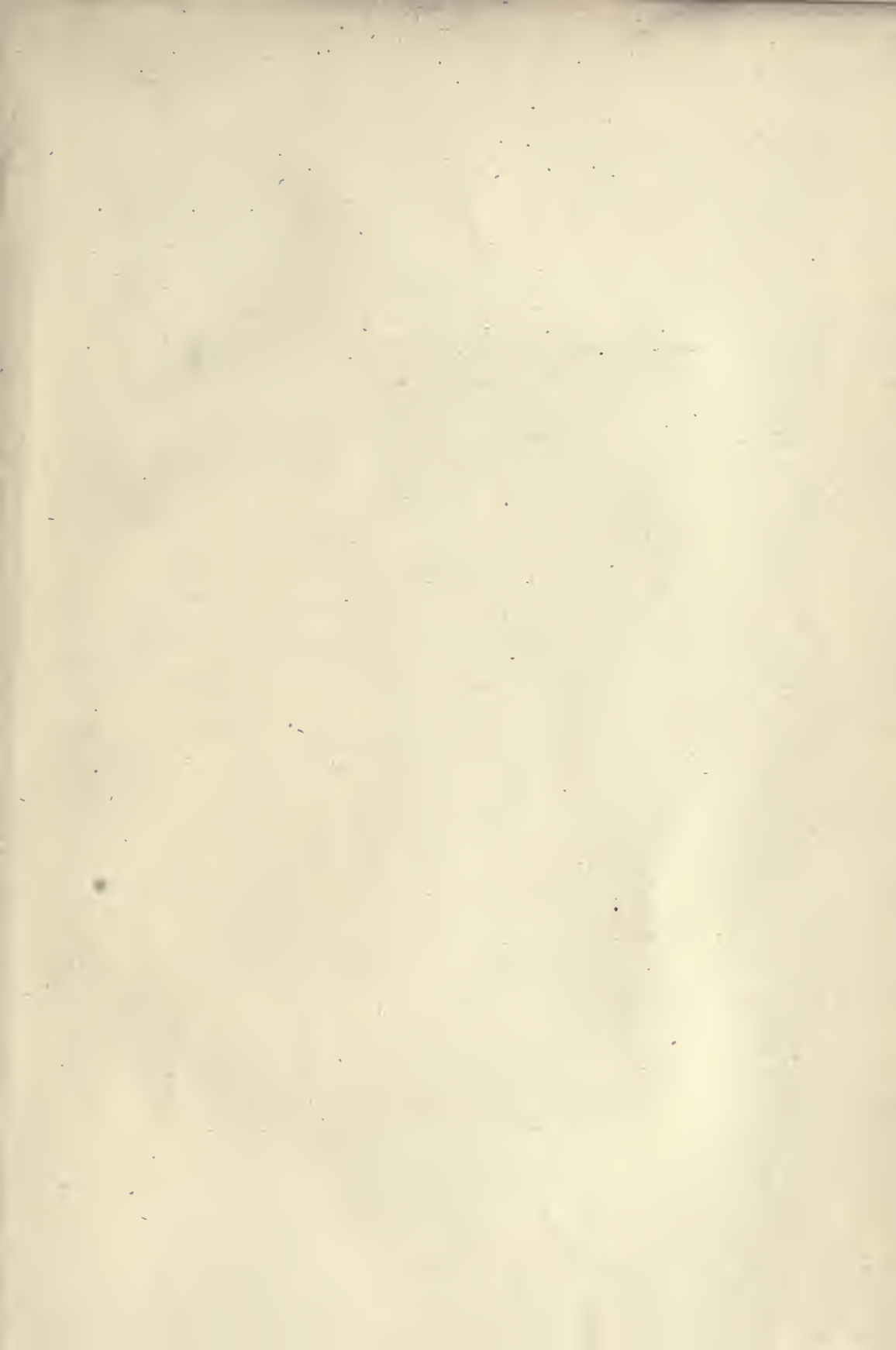
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